PROSPECTIVE STUDY OF HEALTH-RELATED QUALITY OF LIFE IN ADOLESCENT TRANSPLANT RECIPIENTS

by

KATIE ANN DEVINE

(Under the Direction of Ronald L. Blount)

ABSTRACT

With improved survival rates for pediatric transplantation, more attention has turned to children's and adolescents' health-related quality of life (HRQOL), or physical, mental health, and psychosocial well-being. Poorer psychosocial well-being has been related to physical limitations, intensity of side effects, and lower family support (Dew et al., 2001; Glazer, Emery, Frid, & Banyasz, 2002; Meyers, Thomson, & Weiland, 1996; Simons et al., 2007). Additionally, discrepancies have been noted between parent and child report (Levi & Drotar, 1999; Theunissen et al., 1998). Longitudinal studies are needed to identify predictors of HRQOL and changes in HRQOL over time.

The present longitudinal study aimed to expand our understanding of parent versus child reporting of HRQOL and factors related to and predictive of HRQOL over time. Forty-eight adolescents (71% of initial sample; 57% female, 31 kidney, 14 liver, 9 heart) and their parents completed initial and 17-month follow-up assessments.

Results showed that parents and adolescents were generally calibrated to each others' report across HRQOL domains, with the exception of Family Cohesion. However, adolescents reported significantly higher levels of Self-Esteem and General Health Perceptions compared to

their parents. Compared to a normative sample, parents reported lower HRQOL for Physical Functioning, General Health Perceptions, Family Activities, overall Physical Summary, and negative Emotional Impact on themselves.

Most HRQOL domains were stable across time, but both parents and adolescents reported significantly worse General Health Perceptions at Time 2. After controlling for Time 1 levels, Time 2 General Health Perceptions were predicted by adherence for adolescents' reports and side effects for parents' reports. Several medical and family factors were related to adolescent and parent report of HRQOL. After controlling for Time 1 levels, Time 2 Physical Functioning was predicted by hospitalizations for both adolescents' and parents' reports. For Time 2 Mental Health, adolescents' report of side effects and instable immunosuppressant assay levels, and parents' report of side effects plus family cohesion were predictive of Time 2 functioning after controlling for Time 1 levels. Results suggest that improving family cohesion and parent-adolescent relationships may help improve adolescents' HRQOL.

INDEX WORDS: Health-related quality of life; Pediatric transplant; Adolescents

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CHAPTER 1

INTRODUCTION

Health-Related Quality of Life: Significance, Definition, and Measurement

Survival rates for pediatric transplant recipients have dramatically improved in the last few decades, in large part due to advancements in surgical techniques and the effectiveness of immunosuppressant medications (Burdelski et al., 1999; Gummert, Ikonen, & Morris, 1999; OPTN/SRTR, 2006). With improved survival rates, greater attention has been given to children's and adolescents' health-related quality of life (HRQOL), which has been defined as a multidimensional construct including, but not limited to, an individual's physical, mental health, and psychosocial well-being (De Civita et al., 2005; Eiser & Morse, 2001b). In a review of studies evaluating health-related quality of life with pediatric populations, De Civita et al. noted variability in the definition of HRQOL across studies and the importance of delineating HRQOL from quality of life (QOL). In general, QOL is viewed as a broader construct, incorporating at least three core domains of physical, social, and emotional well-being, as recommended by the World Health Organization (1948).

More recently, the World Health Organization Quality of Life Group (1995) defined QOL as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (p. 1405). Inherent in this definition is the view that QOL is subjective and multidimensional. Similarly, HRQOL is viewed as a subjective multidimensional construct. The major difference between HRQOL and QOL is that HRQOL specifically examines the impact of an individual's

health, including the impact of disease, treatment for disease, and health care policy, on an individual's functioning across domains, while QOL examines functioning across all domains of life that may or may not be affected by health/illness (Bonomi, Patrick, Bushnell, & Martin, 2000; Bradlyn et al., 1996; Spieth & Harris, 1996).

Despite variations in definition, HRQOL has been increasingly recognized as an important construct to measure in children and adolescents with chronic health conditions (Eiser & Morse, 2001b; Spieth & Harris, 1996). Many instruments have been developed to evaluate HRQOL (Eiser & Morse; Spieth & Harris). These instruments generally fall into two categories: generic and disease-specific. Generic HRQOL measures assess various domains of HRQOL, such as physical, mental health, social, family, and role (e.g., school) functioning. Generic measures can be administered to different illness populations, and results can be compared across groups. Disease-specific instruments, on the other hand, assess specific symptoms, concerns, and functions related to a particular illness group. Therefore, each instrument is intended to be used with a single population, and results cannot be compared across groups. A variety of disease-specific measures have been developed for different pediatric groups. To date, no disease-specific instrument of HRQOL has been validated for use with pediatric transplant patients, although there has been one study regarding the development of a HRQOL measure specific to children with end-stage renal disease, which includes renal transplant recipients (Goldstein et al., 2006).

Another important consideration in measuring HRQOL relates to who reports HRQOL. Parents often serve as proxy raters for children, but this disregards the child's subjective view of his/her HRQOL (De Civita et al., 2005; Eiser & Morse, 2001a). Further, the reports of children/adolescents often are discrepant from the reports of their parents (Parsons, Barlow,

Levy, Supran, & Kaplan, 1999; Sudan et al., 2004; Sundaram, Landgraf, Neighbors, Cohn, & Alonso, 2007; Theunissen et al., 1998). Parents have reported their children to be more limited in aspects of physical functioning, bodily pain, and role functioning (Levi & Drotar, 1999), in mental health and global quality of life (Parsons et al., 1999), and in their perceptions of their general health (Sundaram et al., 2007) relative to children's report in those HRQOL domains. On the other hand, in one study in the Netherlands, children from a representative sample of the population reported lower HRQOL in the domains of physical complaints, motor functioning, autonomy, cognitive functioning, and positive emotions relative to their parents (Theunissen et al., 1998). The majority of children in the sample were healthy, but the sample also included children who had a temporary illness such as cold, had a chronic illness, or had a chronic and concurrent temporary illness (Theunissen et al.).

Eiser and Morse (2001a) conducted a review of 14 studies that included both parent and child reports of HRQOL. They concluded that there was greater agreement between parent and child report of HRQOL for domains that include observable behavior, such as physical functioning, and less agreement for domains that include non-observable behavior, such as emotional functioning. However, there were several limitations noted in the review. First, agreement was measured using Pearson's product-moment correlations in most studies, a statistic that is limited to covariation of the values rather than numeric agreement of values. Second, a variety of instruments were used to measure HRQOL, and the content of each domain varied across studies, making it difficult to synthesize results from different studies. Third, findings were not consistent across all studies, indicating that conclusions must be interpreted cautiously. Despite these limitations, the authors demonstrated that it is imperative to consider multiple viewpoints of HRQOL when assessing this construct in children and adolescents.

Britto et al. (2004) proposed that it is important to examine the differences between parent and adolescent perceptions of HRQOL in particular because adolescents often share in the decision-making process for treatment and tend to become increasingly responsible for treatment over time. Additionally, the authors noted that HRQOL is increasingly included as an outcome variable in clinical trials; therefore, it is imperative to examine the differences between parent and adolescent report in order to interpret whether those discrepancies occur due to biases in reporting or effects of interventions (Britto et al.).

Britto et al. (2004) examined differences in parent and adolescent report using the Child Health Questionnaire (CHQ; Landgraf, Abetz, & Ware, 1999) in a sample of adolescents with cystic fibrosis. Using the 50-item parent-report form and the 87-item adolescent-report form, they demonstrated that parents reported poorer HRQOL in the domains of general health perceptions, physical function, behavior, and limitations in role function due to physical health. However, when they examined differences in report using only items that were similarly worded across the two forms, the discrepancy in reporting was limited to the general health perceptions domain. This finding is contrary to several other studies that found discrepancies across more domains (Parsons et al., 1999; Sundaram et al., 2007), including one study that examined child and parent report on identically worded CHQ items (Levi & Drotar, 1999).

The findings indicate that it is important to consider the measure of HRQOL when interpreting differences between parents and adolescents. Discrepancies may be indicative of measurement error or true differences in perception. Additionally, discrepancies could be due to developmental issues, as adolescents may perceive themselves to be less vulnerable or susceptible (Britto et al., 2004). Britto et al. also suggested that individual responses are

influenced by personal history and viewpoint, and transplant recipients may re-adjust their expectations of what is considered healthy based on their history of health problems.

Health-Related Quality of Life in Pediatric Transplant Recipients

Taylor, Franck, Gibson, and Dhawan (2005) reviewed studies of HRQOL after pediatric liver transplantation published between 1990 and 2003. Despite initially identifying over 800 studies, only 11 studies met inclusion criteria (i.e., children between 0 and 18 years receiving only a liver transplant and HRQOL assessed in 2 or more of the HRQOL domains). These studies measured HRQOL using different HRQOL instruments or a battery of measures that assessed the different domains of HRQOL. All studies were single-center with small sample sizes. The methodological quality varied across studies, and all but one study were cross-sectional in design. Taylor et al. concluded that HRQOL significantly improved following transplantation, and there was a trend for transplant recipients to report lower HRQOL compared to healthy children, though this was not significant.

Several studies warrant individual discussion. Bucuvalas et al. (2003) examined parent-report of HRQOL in pediatric liver transplant recipients using two measures of HRQOL, the Child Health Questionnaire (CHQ-PF 50) and the PedsQL (Varni, Seid, & Kurtin, 2001). Results indicated lower HRQOL compared to healthy norms for all domains assessed by the PedsQL and for the physical and psychosocial summary scores on the CHQ-PF 50. All of the subscale scores from the CHQ-PF 50 were significantly lower than healthy norms, with the exceptions of mental health, family cohesion, and role functioning. Additionally, the PedsQL subscales of physical health, emotional functioning, and social functioning were comparable to norms for children with chronic illnesses. However, the school functioning and psychosocial health subscales were significantly lower compared to the norms for children with chronic illnesses.

Another study examining parent report on the PedsQL and CHQ-PF 50 for pediatric liver transplant recipients (Fredericks et al., 2007) found that HRQOL was significantly lower than healthy children across all domains on the PedsQL and for the physical and psychosocial summary scores on the CHQ-PF 50. These results were consistent with the study by Bucuvalas et al. (2003). Similarly, all of the subscale scores from the CHQ-PF 50 were significantly lower than healthy norms, with the exceptions of family cohesion and self-esteem. Parents also reported lower scores relative to norms for children with diabetes and cancer on several of the PedsQL domains. Child report on the PedsQL showed a similar pattern, with the exception that emotional functioning was not significantly different from healthy controls or norms for children with diabetes and cancer.

In contrast to Bucuvalas et al. (2003) and Fredericks et al. (2007), Alonso et al. (2003) examined parent-reported HRQOL in pediatric liver transplant recipients using the CHQ-PF 50 and found lower HRQOL relative to healthy norms on the physical summary scale but not the psychosocial summary scale. Additionally, only three subscales were significantly lower compared to healthy norms, including general health perceptions, emotional impact on parents, and disruption of family activities.

Sundaram, Landgraf, Neighbors, Cohn, and Alonso (2007) expanded previous work by examining HRQOL in adolescent liver and kidney transplant recipients using self- and parent-report on the Child Health Questionnaire (CHQ-CF 87 and CHQ-PF 50). Results indicated that adolescents perceived their HRQOL to be lower than healthy norms on the general health perceptions domain, but equivalent across all other domains. Similarly, parents rated adolescents' HRQOL as lower compared to healthy norms in the domains of general health perceptions and physical functioning, but equivalent across other psychosocial domains. Further,

parents reported more negative emotional impact and more limitations on family activities due to their adolescent's health compared to the normative population.

Few studies have examined HRQOL in children with a renal transplant. Goldstein et al. (2006) found that patients with end-stage renal disease (including patients following a kidney transplant and those on dialysis) and their parents reported significantly lower HRQOL compared to healthy children. Children who had received a kidney transplant reported higher HRQOL compared to children on dialysis on the total scale, as well as on the physical health, psychosocial health, and school subscales. Parents of children with a renal transplant reported higher HRQOL across all domains but school functioning. Qvist et al. (2004) found that self-reported global HRQOL, as measured by a 17-dimension HRQOL instrument, was significantly lower for renal transplant recipients compared to healthy children. Examining the profile of HRQOL showed that renal transplant recipients reported lower HRQOL in the areas of school, hobbies, friends, ability to concentrate, sleeping, elimination, breathing, discomfort and symptoms, and speech (Qvist et al.).

Very limited research has examined HRQOL in pediatric heart transplant recipients (Pollock-BarZiv, Anthony, Niedra, Dipchand, & West, 2003). Pollock-BarZiv et al. found that adolescents' report of HRQOL on the PedsQL was equivalent to healthy norms across all subscales. However, the generalizability of this study was limited as the sample size was very small (n = 10) and parent report was not included.

One study that examined HRQOL in renal, liver, and heart transplant recipients relative to healthy controls (Apajasalo, Rautonen, Sintonen, & Holmberg, 1997) found that HRQOL was lower for children aged 8-11 compared to healthy controls, but similar to controls for children aged 12-23. However, the latter group included a wide age range which may have masked any

differences in adolescents versus young adults. This study did not find any relation between type of transplant and HRQOL.

Factors Related to Health-Related Quality of Life in Pediatric Transplant Recipients

Several medical, demographic, and family factors have been examined as potential influences on HRQOL and clinical outcomes in pediatric transplant recipients. Identifying factors that influence HRQOL either positively or negatively provides further understanding of the impact of illness and treatment on pediatric patients and can inform the development of interventions to improve HRQOL. Additionally, HRQOL can serve as an outcome of effectiveness of interventions (De Civita et al., 2005; Eiser & Morse, 2001b).

There have been mixed results regarding the relations between HRQOL and age at transplant, time since transplant, and health status (e.g., number of hospitalizations, number of rejection episodes). One study found significant relations between domains of HRQOL, particularly physical health, and age at transplantation, years since transplantation, and hospitalizations (Bucuvalas et al., 2003). In children less than five years of age, time elapsed since transplant was a significant predictor of functional health (Cole et al., 2004). However, other studies have not replicated these effects, although the possible effects of age and time since transplant are commonly evaluated (Alonso et al., 2003; Fredericks et al., 2007).

Medical disability has been significantly related to physical functioning and general health domains of HRQOL for renal transplant recipients but not liver when using a specific HRQOL measure (Sundaram et al., 2007). Medical disability was not significantly related to HRQOL in liver patients when HRQOL was assessed using a utility index, which is a tool that provides a numeric number for health status based on rating of preference for the specific health state compared with death (Midgley, Bradlee, Donohoe, Kent, & Alonso, 2000). The utility

index used in the study examined domains of sensation, mobility, emotion, cognition, self-care, and pain, and parents reported on the level of functioning for their child in each domain, with more severe scores earning higher overall disability ratings.

Information regarding children's growth, including height and weight converted to standard *Z*-scores, has frequently been examined as potential factors relating to HRQOL, particularly physical functioning. The majority of studies did not find significant relations between HRQOL and height *Z*-scores for liver patients (Alonso et al., 2003; Fredericks et al., 2007; Sundaram et al., 2007), with the exception of one study (Bucuvalas et al., 2003). One study found a strong positive correlation between height *Z*-scores and adolescent ratings of physical functioning and physical role functioning in kidney patients (Sundaram et al., 2007). Thus, although height *Z*-scores may be an indicator of physical health, they do not appear to be consistently strong predictors of HRQOL.

Race has been examined as a potential factor related to HRQOL, with mixed results. Caucasian (vs. Non-Caucasian) race was associated with higher parent report of physical HRQOL in one study (Bucuvalas et al., 2003), but with lower parent report of mental health HRQOL in our previous work (Simons et al., 2007). Race was not associated with HRQOL in other studies (Fredericks et al., 2007; Sundaram et al., 2007). Race is an important factor to consider, as disparities between races could suggest that different factors relate to HRQOL for different groups or indicate cultural biases in measurement of HRQOL.

Race and gender have been related to noncompliance (Meyers, Thomson, & Weiland, 1996), which, in turn, has been linked to poorer HRQOL (Fredericks et al., 2007). Gender has not been found to be significantly associated with HRQOL in several studies (Bucuvalas et al., 2003; Cole et al., 2004; Fredericks et al., 2007; Sundaram et al., 2007). However, one study

showed that parents of liver transplant recipients younger than five years old rated boys as higher on several HRQOL domains, including general health, global health, and the emotional and time impact of the condition on parents (Cole et al., 2004). In another study, gender influenced self-perceptions, self-worth, social competence, and behavioral problems in adolescent transplant recipients (Tornqvist et al., 1999). In that study, boys perceived themselves as less competent related to physical appearance, athletic abilities, romantic appeal, scholastic cognitive abilities, behavioral conduct, and global self-worth. Girls perceived themselves as less competent related to scholastic cognitive abilities, athletic abilities, and job skills. Therefore, gender may influence how parents rate their children and how children perceive themselves. Although most studies have not found relations between gender and HRQOL, the few investigations that found differences suggest that it is important to evaluate for gender differences to better understand the impact of transplantation on HRQOL.

Other demographic variables studied include marital status and maternal education. In an investigation of HRQOL in children with end-stage renal disease (Goldstein et al., 2006), children with married parents reported higher HRQOL in the emotional functioning domain compared to children with parents who were not married. Parents who were married reported children's HRQOL to be higher in the emotional functioning, school functioning, and psychosocial health domains. Marital status of parents was not significantly related to HRQOL in our previous study (Simons et al., 2007). Maternal education was a significant predictor of physical and psychosocial HRQOL in one study (Bucuvalas et al., 2003). Mothers with education above high school reported higher social function HRQOL for their adolescents versus mothers with a high school education or less. One limitation was that maternal education may be a proxy for socioeconomic status, and Bucuvalas et al. did not evaluate the effects of

socioeconomic status. The inconsistent results in the literature warrant further exploration of these factors, as parental marital status and education level may serve as risk or resilience factors for positive child adaptation following transplant.

Family factors are important to consider given that adolescents live within the context of their families, and family members are often involved in or affected by treatment in some way. In our previous research (Simons et al., 2007), family conflict and perceived frequency of side effects were significant predictors of lower adolescent-reported physical functioning and mental health HRQOL outcomes. Compared to normative samples, Fredericks et al. (2007) found that family cohesion and conflict were similar to published norms on the Family Assessment Device and Family Environment Scales, two widely-used family instruments, suggesting that the amount of conflict and cohesion in families of liver transplant recipients is not different from families of healthy children. Fredericks et al. did not evaluate the relationship between HRQOL and family cohesion and conflict; however, they did examine family factors related to adherence and adherence related to HRQOL. The rate of clinic attendance was positively related to family cohesion (measured via HRQOL scale) and family problem-solving. Thus, family factors may influence adherence behaviors, such as clinic attendance and medication-taking, which in turn influence HRQOL.

Adherence to immunosuppressant medications is an important factor to consider in relation to HRQOL for pediatric transplant recipients, as nonadherence to these medications has been linked to serious negative health outcomes, including rejection episodes, hospitalizations, allograft loss, and death (Falkenstein, Flynn, Kirkpatrick, Casa-Melley, & Dunn, 2004). Indeed, Fredericks et al. (2007) found that nonadherence measured by clinic attendance rate of less than 80% was significantly related to lower physical HRQOL reported by parent. Further, Fredericks

et al. classified adolescents as nonadherent based on tacrolimus (a specific immunosuppressant drug) standard deviation, and a higher standard deviation indicated greater drug level instability and variability in medication-taking. Parents of adolescents classified as nonadherent reported significantly more role/social limitations due to emotional/behavioral difficulties for their adolescents. Parents of nonadherent adolescents also reported higher emotional impact on themselves, as well as lower family cohesion relative to parents of adolescents classified as adherent. Given that estimates of nonadherence rates for pediatric populations are high (around 50%), particularly among adolescents (DiMatteo, 2004b; Rapoff, 1999; Rianthavorn, Ettenger, Malekzadeh, Marik, & Struber, 2004), it is imperative to further understand the relations among nonadherence, HRQOL, and family factors.

Several studies have examined relations between nonadherence and family factors. A meta-analysis that included 14 studies of family cohesiveness and adherence to medical regimens found higher family cohesiveness was related to higher adherence (DiMatteo, 2004a; Rapoff, 1999). In that analysis, DiMatteo examined six studies of family conflict and adherence and found that poorer adherence was associated with greater family conflict. Although there appear to be significant relations between family cohesiveness, conflict, adherence, and HRQOL, these factors have not been thoroughly evaluated within the same study, with the exception of Fredericks et al. (2007).

There are several limitations within the current literature. Although several studies have found discrepancies between parent and child reports of HRQOL (Britto et al., 2004; Parsons et al., 1999; Sudan et al., 2004; Sundaram et al., 2007), the domains and magnitude of differences have been inconsistent and warrant further analysis. Similarly, several studies have shown differences between reports of HRQOL for transplant recipients compared to healthy norms

(Alonso et al., 2003; Bucuvalas et al., 2003; Sundaram et al., 2007), but again findings have been inconsistent across domains of HRQOL.

Additionally, findings related to medical, demographic, and family factors have been inconsistent. Family factors have been associated with adherence, which, in turn, has been associated with HRQOL, but very limited research has examined all of these factors simultaneously (Fredericks et al., 2007). Examining medical, family, and adherence factors together will allow for better understanding of the relations among these variables.

Another limitation is that the majority of studies have examined HRQOL in liver transplant recipients, with limited inclusion of kidney and heart transplant recipients. The majority of studies are cross-sectional in nature, making it difficult to infer causal relationships among factors related to HRQOL. Longitudinal studies are needed to identify predictors of HRQOL and changes in HRQOL over time.

Purpose of Present Study

The present study aimed to prospectively examine the relations between HRQOL and medical, demographic, and family factors in adolescent kidney, liver, and heart transplant recipients at an initial and 17-month follow-up time point. This study included parent- and self-report of HRQOL, family functioning, adherence, and medical factors to provide a comprehensive assessment of these adolescents and examine differences in self versus parent report. This longitudinal study was unique in its inclusion of three organ types. This study recruited from an initial sample of 68 adolescent-parent dyads who participated in a cross-sectional investigation conducted through Children's Healthcare of Atlanta in 2006. The goal of this longitudinal research was to elucidate relations among HRQOL and medical, demographic,

and family factors to identify areas for intervention to improve long-term HRQOL in adolescent transplant recipients.

Hypotheses

First, we expected significant intra-class correlations between adolescent and parent report of the adolescent's health-related quality of life at Time 1 and Time 2 for physical domains of HRQOL, but not for psychosocial domains.

Second, we expected that adolescents would report higher HRQOL relative to their parent's report. We also hypothesized that parent-report of adolescent HRQOL will be lower than normative data for healthy adolescents, particularly on physical domains.

Third, we hypothesized that specific medical and family factors would predict HRQOL at Time 2. Specifically, we hypothesized that more medication side effects, adverse clinical outcomes, including rejection episodes and hospitalizations, and lower family cohesion would be significant predictors of lower physical and mental health HRQOL at Time 2.

CHAPTER 2

METHOD

This investigation included 17-month longitudinal data collected on two occasions from a sample of adolescents who have received a solid organ transplant (kidney, liver, heart). The measures and procedures were those used in our previous research (Simons & Blount, 2007), with some additional measures added for this follow-up investigation.

Participants

Our initial study involved 68 (56% male) solid organ transplant recipients (39 kidney, 17 liver, 12 heart) and their parent/guardian. Forty-eight adolescent-parent dyads (71% of original sample; 56% female, 28 kidney, 13 liver, 7 heart) completed 17-month follow-up assessments. Four adolescents (6%) died during the follow-up period. Nine adolescents or parents (13%) participated, but we were unable to enroll both parts of the dyad and therefore did not use their data in these analyses. Seven (12%) were unable to be contacted for re-enrollment. Excluding the adolescents who could not be re-enrolled due to mortality, our present participation rate was 77%. There were no systematic differences between dyads who were re-enrolled versus those who could not be enrolled in terms of demographic information, with the exception that girls were more likely to be re-enrolled ($\chi^2 = 9.74$, $p < .01$).

In this sample, participants were predominantly Caucasian (60%) or African American (29%). Participants' age ranged from 12.5 – 22.4 years ($M = 17.1$, $SD = 2.4$). Time since transplant ranged from to 1.5 to 17.9 years ($M = 7.2$, $SD = 5.1$). Follow-up interviews were conducted an average of 17.0 months after the initial interview ($SD = 1.5$, range = 12 to 20

months). Inclusion criteria for the initial study were having received a solid organ transplant at least 6 months prior to the study, age of at least 11 years, living at home with parent(s)/guardian(s), and being English-speaking. Exclusion criteria included being diagnosed with a developmental delay or a psychotic disorder.

Procedures

This investigation was approved by the Institutional Review Boards of Emory University/Children's Healthcare of Atlanta and the University of Georgia. The 68 participants from our initial study were contacted using multiple recruitment methods to assess their interest in participating in the longitudinal aspect of this study and obtain informed consent/assent. We attempted to contact patients and families via: (a) telephone; (b) outpatient clinic appointments; and/or (c) mail. Given our success with phone interviews during the initial assessment and the ease of phone interviews for patients, we conducted phone interviews with participants to complete all measures. We offered to schedule in-person interviews if preferred by patients/families, but no patients requested this method.

When participants and parents were contacted, either in person or via phone, the study was described and written or verbal informed consent and assent were obtained. If contacted via mail, families received a written description of the study and consent/assent forms to return in a pre-paid envelope. If verbal informed consent was obtained via telephone, written consent was then obtained via mail. Interviews were scheduled following this procedure and conducted via telephone at a time convenient for the adolescent and parent/guardian.

Each interview was conducted by trained research assistants. Parent interview length ranged from 35 to 100 minutes (M = 58.5, SD = 15.4) and adolescent interview length ranged from 25 to 60 minutes (M = 36.9, SD = 7.5).

Measures

The main variables of interest included health-related quality of life, family functioning, and medical factors (i.e., medication adherence, side effects, disease and medical regimen factors, and clinical outcomes). Demographic factors were also collected.

Health-Related Quality of Life: (1) Adolescent Self-Report. The Child Health Questionnaire- Child Form 87 (CHQ-CF87; Landgraf et al., 1999) is an 87-item scale assessing health-related quality of life in adolescents 12 to 18 years of age. Each item consists of five response choices using a likert-like rating scale. Eight subscales were administered, including: physical functioning, bodily pain, general behavior, mental health, self esteem, general health perceptions, family activities, and family cohesion. Promising reliability data exist for this measure; however, published normative data have been limited to item means and not subscale means. Additionally, the normative sample consisted of inner-city African American youth (N = 263), which is not representative of the population. The publishers recognize that this is not a representative sample. Within this sample and three clinical samples (attention-deficit/hyperactivity disorder, cystic fibrosis, and end stage renal failure), Cronbach alpha coefficients exceeded the minimum .70 conventional standard (Nunnally & Bernstein, 1994) for six of the eight subscales across the samples (the alpha coefficient for General Health Perceptions was below .70 in three out of four samples and an alpha coefficient cannot be calculated for the family activities subscale as it contains only one item). Alpha coefficients ranged from .63 to .89 in the school-based African American sample and from .62 to .97 in the three clinical samples. In the present sample, alpha coefficients ranged from .70 to .88 for Time 1 data and from .59 to .90 for Time 2 data. All coefficients exceeded the minimum .70 standard except Time 2 physical functioning.

(2) Parent Report of Adolescent's Quality of Life. The Child Health Questionnaire-Parent Form 50 (CHQ-PF50; Landgraf et al., 1999) is a 50-item scale assessing health-related quality of life in children ages 5 to 18. Of note, 8 of our participants were outside of this age range at Time 2, but we utilized the measure to allow for comparison with Time 1 data. Parents completed the same eight subscales as their children did (physical functioning, bodily pain, general behavior, mental health, self esteem, general health perceptions, family activities, and family cohesion), plus two additional scales measuring the impact of the child's condition on the parent's time and emotional functioning: parental impact – emotional, and parental impact – time. The CHQ-PF50 also yields two summary scales, physical summary and psychosocial summary.

Extensive reliability and validity data exist for the CHQ-PF50 and it is used frequently in pediatric populations. The normative sample ($N = 391$) is representative of the general US population (Landgraf et al., 1999). Cronbach alpha coefficients ranged from .66 to .94 in the normative sample, and from .56 to .98 in six clinical samples (asthma, cystic fibrosis, epilepsy, juvenile rheumatoid arthritis, attention-deficit/hyperactivity disorder, and psychiatric disorder). Cronbach alpha coefficients for six of the eight subscales that were administered in this study met or exceeded the minimum standard of .70 in the normative sample (the alpha coefficient for the General Health Perceptions subscale was .66 and alpha coefficient could not be calculated for the 1-item family cohesion scale). Cronbach alpha coefficients for the summary scales were excellent at .93 for both the physical and psychosocial summary scales in the normative population. The alpha coefficients for the summary scales in the clinical samples were also good, ranging from .84 to .97 for the physical summary scale ranged and .88 to .97 for the psychosocial summary scale.

In the present sample, alpha coefficients ranged from .41 to .91 for Time 1 data and from .62 to .90 for Time 2 data. Several coefficients fell below the minimum standard of .70, including Time 1 behavior (α = .60), mental health (α = .69), general health perceptions (α = .52), and parental impact – time (α = .41), as well as Time 2 general health perceptions (α = .62). Cronbach alphas for the summary scales were good at .73 for both for Time 1 and .86 for both for Time 2.

Family Functioning: (1) Family Relationship Index (Moos & Moos, 1994). The FRI is a subset of the Family Environment Scale (FES), consisting of 3 of the 10 subscales: conflict, expressiveness, and cohesion. Each subscale contained 9 true-false items, and the combined 27-item index was used to assess the overall quality of family relationships. Adequate internal consistencies of .78, .69, and .85, and two-month test-retest reliabilities of .86, .73, and .85, respectively, have been reported for the three subscales of the FRI (Moos & Moos, 1994). For this investigation, only the conflict and cohesion subscales were utilized. In the present sample, Cronbach alphas for parent cohesion and conflict were below the acceptable standard of .70 for both Time 1 and Time 2 (α = .44 to .68). The alpha coefficient for adolescent cohesion was acceptable at Time 2 (α = .72), but fell below the standard for Time 1 (α = .59). Cronbach alpha coefficients for adolescent conflict were below the accepted standard at Time 1 and 2 (α = .61 and .66, respectively).

(2) Stress Index for Parents of Adolescents (Sheras, Abidin, & Konold, 1998). Parents completed one subscale from the SIPA: Adolescent-Parent Relationship Domain (APRD). The APRD consists of 16 items and each item is scored on a 5-point likert scale from strongly disagree to strongly agree. This subscale measured parents' perceived quality of relationship between parent and adolescent. Higher scores indicate more problematic relationships. The

APRD subscale has demonstrated excellent internal consistency (α = .91) and one-month test-retest reliability of .91 (Sheras et al., 1998). In the present sample, Cronbach alpha was excellent at .91.

Medical Factors: (1a) Adherence: Parent and Self-Report. The Medical Adherence Measure Medication Module (Zelikovsky & Schast, in press) assesses knowledge of medication name, purpose, dosage amount, and dosage frequency. It requires parents and adolescents to independently report how many doses of each medication were missed in the past 7 days. Keeping the recall period short and asking detailed objective questions has been described as an effective way to obtain self-reported adherence (La Greca & Bearman, 2003). Percent adherence was calculated by taking the number missed doses divided by number prescribed, times 100.

(1b) Adherence: Immunosuppressant Drug Assay Levels. Immunosuppressant blood levels collected during the 17-month period since the patient's initial interview date were recorded from the medical chart. For patients prescribed tacrolimus ("tacro;" a specific immunosuppressant medication), standard deviations (SD) were calculated from the results of the blood assays. A SD outside of 3 was considered out-of-range, consistent with guidelines proposed by Shemesh et al. (2004). A higher SD signifies a higher degree of difference among individual levels, indicating higher instability in medication levels. Higher instability suggests less consistent medication taking or lower adherence. However, medication blood levels may vary as a result of acute illness or implementation of a more aggressive treatment. Therefore, only levels that were obtained in the outpatient clinic during routine visits were analyzed. Higher SDs have been found to be predictive of clinical outcomes, including biopsy-proven rejection episodes (Shemesh et al., 2004).

(2) Perceived Side Effects. The End-Stage Renal Disease Symptom Checklist-Transplant Module (ESRD-SCL; Franke et al., 1999), validated for use with adults, was adapted for use with this sample. The adapted scale measured the frequency of 39 different side-effects (e.g., weight gain, bruising) on a 5-point Likert-like scale, and yielded a total frequency score. This measure was completed by adolescents and parents. Adequate construct validity and internal consistency have been demonstrated for the ESRD-SCL. Cronbach alpha coefficients for frequency of side-effects were good at Time 1 and Time 2 for both adolescent and parent report ($\alpha = 0.74$ to .87).

(3) Clinical Outcomes: Data were obtained from medical records on: (a) transplant type, (b) date of transplant(s), (c) presence of rejection episode, (d) number of hospitalizations, and (e) current medications and dosage. Given the variability of time between assessments (range of 12 to 20 months), the number of hospitalizations was standardized by dividing the total number of hospitalizations by the number of months between assessments. This ensured that an individual who had a longer period of time between assessments would not be penalized for a greater number of hospitalizations due to length of time. These outcome data were important as acute rejection has been found to be associated with low immunosuppressant drug levels and subsequent chronic rejection (Feinstein et al., 2005).

Demographic Information. Demographic information collected about the adolescent included: (a) age, (b) gender, and (c) race. Demographic information collected about the parent included: (a) marital status, (b) educational attainment, and (c) income.

CHAPTER 3

RESULTS

Overview of Data Analyses

Domains of health-related quality of life were the main dependent variables of interest. Preliminary analyses examined relationships between demographic variables, disease variables, and HRQOL. Analyses focused on the following areas: (a) relationship between adolescent and parent report of HRQOL at both time periods, measured via Pearson product-moment correlations, intra-class correlations, and dependent t-tests; (b) changes in domains of HRQOL over time using dependent t-tests; and (c) relations among medical and family factors and specific domains of HRQOL using Pearson correlations, as well as prediction of HRQOL domains at the follow-up period using hierarchical regression analyses. For the latter analyses, the HRQOL domains of Physical Functioning, Mental Health, and General Health Perceptions were selected.

Demographics, Disease Variables, and HRQOL

There were no significant correlations between age, gender, parent educational attainment, time since transplant, and HRQOL domains at Time 1 and Time 2. Also, there were no differences in HRQOL domains by parent marital status (married vs. not married). Additionally, there were no significant differences across domains of HRQOL among organ groups, and so all participants were grouped together for the remainder of analyses. However, there were significant correlations between income and Time 2 adolescent-reported Physical Functioning ($r = .32$, $p < .05$) and parent-reported General Health Perceptions ($r = -.37$, $p < .05$).

Further, there were differences between races (Caucasian vs. Non-Caucasian) for Time 2 report (but not Time 1) on three subscales of HRQOL: parent-reported Self-Esteem and Bodily Pain and adolescent-reported Self-Esteem. At the follow-up assessment, parents of Non-Caucasian adolescents reported significantly higher functioning in regards to Bodily Pain (M = 85.78, SD = 26.10, $F(1,46) = 4.38$, $p = .04$, $\omega = .26$) and Self-Esteem (M = 82.24, SD = 19.24, $F(1,46) = 5.18$, $p = .03$, $\omega = .28$) compared to parents of Caucasian adolescents (M = 70.34, SD = 24.27, and M = 68.48, SD = 21.23, respectively). Non-Caucasian adolescents reported significantly higher Self-Esteem compared to Caucasian adolescents (M = 87.57, SD = 10.95 for Non-Caucasian, M = 80.09, SD = 12.98 for Caucasian, $F(1,46) = 4.29$, $p = .04$, $\omega = .25$). Demographic variables were not considered in further analyses of HRQOL, with the exception of income for Time 2 adolescent-reported Physical Functioning and parent-reported General Health Perceptions, and race for analyses including Time 2 parent-reported Bodily Pain and Self-Esteem and adolescent-reported Self-Esteem.

Adolescent versus Parent Report

At Time 1 and Time 2, the agreement between adolescent and parent report was examined via intraclass correlations (Shrout & Fleiss, 1979). Pearson product-moment correlations were also calculated. As can be seen in Tables 1 and 2, significant intraclass correlations between adolescent and parent report were found for all HRQOL domains at Time 1 except Family Cohesion and for all HRQOL domains at Time 2 except Bodily Pain and Family Cohesion. The Pearson correlations followed a similar pattern.

For each domain, the mean report of adolescents and parents were compared using dependent t-tests. Table 1 shows the results at Time 1. Results show that adolescents reported significantly higher functioning in the domains of Self-Esteem and General Health Perceptions

compared to their parents. Parents reported higher levels of Family Cohesion at a trend level. At Time 2, a similar pattern of results emerged (see Table 2). Again, adolescents reported significantly higher Self-Esteem and General Health Perceptions compared to their parents. They also reported significantly higher Physical Functioning. Additionally, parents reported higher Family Cohesion at a trend level. In prior analyses, race differences were noted for three Time 2 HRQOL domains (parent-reported Bodily Pain and Self-Esteem and adolescent-reported Self-Esteem). Therefore, interaction effects for race x reporter were examined, but there were no significant interactions.

Parent Report Compared to CHQ-PF50 Norms

Table 3 shows parent report of HRQOL domains at Time 1 relative to the published normative data for the CHQ-PF50. Results indicated that parents reported significantly lower functioning for their adolescents on several domains of HRQOL, including Physical Functioning, Self-Esteem, General Health Perceptions, Family Activities, and Physical Summary. These differences demonstrated medium to large effect sizes (*r* ranged from .30 to .83). Parents reported significantly higher Family Cohesion relative to norms. Parents also reported significantly worse Emotional Impact on themselves due to their child's health relative to norms.

Results at Time 2 were similar to those at Time 1. Parents reported significantly lower functioning for their adolescents on the HRQOL domains of Physical Functioning, General Health Perceptions, Family Activities, and Physical Summary (see Table 4). These differences demonstrated medium to large effect sizes (*r* ranged from .44 to .84). Unlike Time 1, there was no significant difference between average parent report of Self-Esteem ($M = 73.92$, $SE = 3.08$) and the normative mean Self-Esteem ($M = 79.8$, *SE* not reported). Similar to Time 1, parents

reported significantly higher Family Cohesion as well as significantly worse Emotional Impact on themselves due to their child's health relative to the normative sample.

Change in HRQOL from Time 1 to Time 2

Table 5 shows changes in mean adolescent report of HRQOL from Time 1 to Time 2. On average, adolescents reported significantly lower General Health Perceptions at Time 2 compared to Time 1. However, adolescents reported similar functioning for all other domains of HRQOL at both time periods. Additionally, Pearson correlations between the Time 1 and Time 2 levels of each domain were significant for all domains except Family Cohesion.

Changes in mean parent report of HRQOL for Time 1 and Time 2 are shown in Table 6. On average, parents reported significantly lower General Health Perceptions at Time 2 compared to Time 1. On the other hand, they reported significant improvements in their own Emotional Impact due their child's health from Time 1 to Time 2. On average, parents reported similar functioning for all other domains of HRQOL at both time periods. Additionally, Pearson correlations between the Time 1 and Time 2 levels of each domain were significant for all domains except Bodily Pain, Family Activities, Role/Social Limitations due to Physical Problems, and Role/Social Limitations due to Emotional/Behavioral Problems.

Medical and Family Factor Predictors of HRQOL

The domains of Physical Functioning, Mental Health, and General Health Perceptions were further analyzed since physical functioning and mental health are seen as key components of HRQOL and general health perceptions demonstrated change over time in this sample. First, Pearson product-moment correlations were calculated between medical and family factor predictors and the Time 2 Physical Functioning, Mental Health, and General Health Perceptions for adolescent- and parent-reports (see Tables 7 and 8). Next, hierarchical regression equations

were calculated to predict Time 2 level of functioning for the three HRQOL domains. Equations were calculated separately for adolescents and parents (see Tables 9-11).

For adolescents, Time 1 side effects and hospitalizations since Time 1 were significantly negatively correlated with Time 2 Physical Functioning (see Table 7). Adherence was positively correlated with Physical Functioning. For parents, hospitalizations since Time 1 and Time 2 side effects were negatively correlated with Physical Functioning (see Table 8).

Table 7 shows that Time 2 Mental Health was negatively associated with Time 1 side effects, Time 1 out-of-range Tacro SD, Time 2 family conflict, and Time 2 side effects for adolescents. Further, Time 2 family cohesion and adherence were positively associated with Mental Health. For parents, a similar pattern appeared for Time 1 side effects, Time 2 family conflict, Time 2 family cohesion, and Time 2 side effects (see Table 8). One additional variable of interest was parents' report of the quality of their relationship with their adolescent (Time 2 Adolescent-Parent Relationship Domain). The negative correlation suggested that a better quality relationship was associated with better Mental Health.

For adolescents, Time 2 General Health Perceptions were negatively correlated with Time 1 side effects, Time 2 family conflict, and Time 2 side effects. Adherence was positively correlated with General Health Perceptions (see Table 7). For parents, Time 2 General Health Perceptions were negatively correlated with Time 1 and Time 2 side effects, as well as hospitalizations since Time 1 (see Table 8).

Based on the correlational analyses and previous literature, hierarchical regression equations were conducted to predict Time 2 HRQOL for Physical Functioning, Mental Health, and General Health Perceptions using medical and family predictors. Only those variables that were significantly correlated with the HRQOL domains were considered for inclusion in the

regression analyses. In each equation, baseline levels of the outcome variable were entered in the first step, and medical and family predictors were entered in the second step. The model was trimmed by removing variables that were not significant after each step. Equations were constructed separately for adolescent and parent reports.

For adolescent-reported Physical Functioning, Time 1 levels of Physical Functioning were entered first to control for baseline levels. Additionally, income was entered in the first step, as it was significantly correlated with Time 2 Physical Functioning. In the second step, negative medical outcomes, including hospitalizations since the Time 1 assessment and Time 1 side effects, were entered. Table 9 shows the final model, which included Time 1 Physical Functioning and income at step 1 and hospitalizations at step 2. As can be seen in Table 9, hospitalizations since Time 1 adds a significant 23% of variance above baseline levels of Physical Functioning and income, and the final model accounts for 54% of variance in adolescent-reported Physical Functioning at Time 2 ($\Delta R^2 = .23$, $R^2 = .54$, $F(3,37) = 14.24$, $p < .01$).

For parent-reported Physical Functioning, Time 1 Physical Functioning was entered in step 1 to control for baseline levels, and hospitalizations since Time 1 and Time 2 side effects were entered in step 2. Table 9 shows that hospitalizations since Time 1 added 16% of variance above baseline levels, and the final model accounted for 50% of variance in parent-reported Physical Functioning at Time 2 ($\Delta R^2 = .16$, $R^2 = .50$, $F(2,39) = 19.51$, $p < .01$).

For adolescent-reported Mental Health, adolescent-reported Time 1 Mental Health was entered at step 1, and Time 1 Tacro SD range, Time 2 side effects, and Time 2 family conflict were entered at step 2. As shown in Table 10, the trimmed model consisted of Time 1 Mental Health at step 1 and Time 1 Tacro SD range and Time 2 side effects at step 2. Side effects and

tacro range added a significant 36% of variance above the baseline model, and the final model accounted for 61% of variance in adolescent-reported Mental Health at Time 2 (ΔR^2 = .36, R^2 = .61, $F(3,32) = 16.53$, $p < .01$). For parent-reported Mental Health, parent-reported Time 1 Mental Health was entered at step 1, and Time 2 family cohesion and Time 2 side effects were entered at step 2. As shown in Table 10, the final model consisted of the same variables as entered. Family cohesion and side effects contributed a significant 23% of variance above baseline levels of mental health, and the final model accounted for 59% of variance in parent-reported Mental Health at Time 2 (ΔR^2 = .23, R^2 = .59, $F(3,44) = 20.79$, $p < .01$).

For adolescent-reported General Health Perceptions, Time 1 General Health Perceptions was entered first to control for baseline levels. Time 2 side effects, Time 2 % adherence, and Time 2 conflict were entered in the second step. The trimmed model consisted of Time 1 General Health Perceptions at Step 1 and Time 2 % adherence at step 2 (see Table 11). Adherence accounted for a significant 11% of variance above baseline levels of General Health Perceptions, and the final model accounted for 49% of variance in adolescent-reported General Health Perceptions at Time 2 (ΔR^2 = .11, R^2 = .49, $F(2,45) = 21.25$, $p < .01$). For parent-reported General Health Perceptions at Time 2, Time 1 General Health Perceptions and income were entered at step 1 to control for baseline levels of those two variables. Hospitalizations since Time 1 and Time 2 side effects were entered in the second step. As seen in Table 11, Time 2 side effects added a significant 3% of variance at step 2 at a trend level, and the final model accounted for 61% of variance in parent-reported General Health Perceptions at Time 2 (ΔR^2 = .03, R^2 = .61, $F(3,43) = 22.12$, $p < .01$).

In summary, various medical and family factors were significantly correlated with adolescent and parent report of physical functioning, mental health, and general health

perceptions HRQOL at Time 2, suggesting dynamic relationships among medical and psychosocial factors. Medical factors, including hospitalizations, side effects, tacro SD range, and self-reported adherence were significant predictors of Time 2 physical functioning and general health perceptions HRQOL for both adolescent and parent reports. Medical factors were also significant predictors of adolescent-reported mental health, while a combination of family and medical factors predicted parent-reported mental health at follow-up.

Table 1.

Time 1 Adolescent versus Parent Report of Health-Related Quality of Life.

Health-Related Quality of Life Domain	Adolescent Mean	Parent Mean	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*	*Pearson r*	*ICC*
Physical Functioning	91.90	89.58	2.31 (-2.83 to 7.46)	.91	.13	.42**	.38**
Bodily Pain	80.00	79.58	.42 (-6.87 to 7.70)	.12	.02	.52***	.52***
Behavior	78.71	75.31	3.41 (-.89 to 7.71)	1.59	.23	.40**	.39**
Mental Health	76.75	76.04	.72 (-3.59 to 5.02)	.33	.05	.40**	.40**
Self-Esteem	81.22	74.97	6.23 (1.92 to 10.60)	2.90**	.40	.50***	.46***
General Health Perceptions	59.64	50.38	9.26 (4.64 to 13.89)	4.03***	.51	.38**	.32**
Family Activities	79.43	79.86	-.43 (-7.31 to 6.44)	-.13	.02	.25^{+}	.25*
Family Cohesion	71.67	79.69	-8.02 (-16.96 to .92)	-1.81^{+}	.26	.21	.20^{+}

Note. *p <.05, **p < .01, ***p < .001, ^{+}p < .10.

Table 2.

Time 2 Adolescent versus Parent Report of Health-Related Quality of Life.

Health-Related Quality of Life Domain	Adolescent Mean	Parent Mean	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*	*Pearson r*	*ICC*
Physical Functioning	93.06	85.53	7.52 (1.44 to 13.61)	2.49*	.34	.33*	.22*
Bodily Pain	77.71	76.46	1.25 (-7.44 to 9.94)	.29	.04	.24	.24^{+}
Behavior	74.49	78.73	-4.24 (-9.47 to .99)	-1.63	.23	.33*	.32**
Mental Health	74.97	74.14	.83 (-3.54 to 5.19)	.38	.06	.55***	.54***
Self-Esteem	83.05	73.92	9.13 (3.38 to 14.88)	3.19**	.42	.42**	.33**
General Health Perceptions	55.63	46.32	9.31 (3.95 to 14.68)	3.49***	.45	.34*	.30**
Family Activities	78.13	80.64	-2.52 (-8.59 to 3.55)	-.83	.12	.36*	.36**
Family Cohesion	74.58	82.40	-7.81 (-16.33 to .70)	-1.85^{+}	.26	.19	.18^{+}

Note. *p <.05, **p < .01, ***p < .001, ^{+}p < .10.

Table 3.

Time 1 Parent Report of Health-Related Quality of Life versus CHQ-PF50 Norms.

Health-Related Quality of Life Domain	Time 1 Parent Mean	CHQ-PF50 Norms	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*
Physical Functioning	89.58	96.1	-6.52 (-12.09 to -.94)	-2.35*	.32
Bodily Pain	79.58	81.7	-2.12 (-9.99 to 5.76)	-.54	.08
Behavior	75.31	75.6	-.29 (-4.31 to 3.73)	-.14	.02
Mental Health	76.04	78.5	-2.46 (-6.63 to 1.71)	-1.19	.17
Self-Esteem	74.97	79.8	-4.83 (-9.40 to -.27)	-2.13*	.30
General Health Perceptions	50.38	73.0	-22.62 (-27.06 to -18.17)	-10.24***	.83
Family Activities	79.86	89.7	-9.84 (-15.98 to -3.70)	-3.22**	.43
Family Cohesion	79.69	72.3	7.39 (.96 to 13.81)	2.31*	.32
Role/Social - Physical	92.01	92.5	-6.74 (-14.07 to .60)	-1.85	.26
Role/Social - Emotional/Behavioral	92.59	93.6	-1.01 (-6.26 to 4.25)	-.39	.06
Parental Impact - Emotional	58.65	80.3	-21.65 (-29.68 to -13.63)	-5.43***	.62
Parental Impact - Time	88.92	87.8	1.12 (-3.40 to 5.64)	.50	.07
Physical Summary	47.30	53.0	-5.70 (-8.76 to -2.63)	-3.74***	.48
Psychosocial Summary	49.40	51.2	-1.80 (-3.96 to .36)	-1.68	.24

Note. *p <.05, **p < .01, ***p < .001.

Table 4.

Time 2 Parent Report of Health-Related Quality of Life versus CHQ-PF50 Norms.

Health-Related Quality of Life Domain	Time 2 Parent Mean	CHQ-PF50 Norms	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*
Physical Functioning	85.53	96.1	-10.57 (-16.97 to -4.17)	-3.32**	.44
Bodily Pain	76.46	81.7	-5.24 (-12.75 to 2.28)	-1.40	.20
Behavior	78.73	75.6	3.13 (-1.23 to 7.49)	1.45	.21
Mental Health	74.14	78.5	-4.36 (-9.35 to .63)	-1.76	.25
Self-Esteem	73.92	79.8	-5.88 (-12.08 to .33)	-1.91	.27
General Health Perceptions	46.32	73.0	-26.68 (-31.70 to -21.66)	-10.69***	.84
Family Activities	80.64	89.7	-9.06 (-14.54 to -3.58)	-3.32**	.44
Family Cohesion	82.40	72.3	10.10 (3.56 to 16.63)	3.11**	.41
Role/Social - Physical	85.76	92.5	-6.74 (-14.07 to .60)	-1.85	.26
Role/Social - Emotional/Behavioral	94.44	93.6	.84 (-3.86 to 5.55)	.36	.05
Parental Impact - Emotional	69.27	80.3	-11.03 (-18.40 to -3.66)	-3.01**	.40
Parental Impact - Time	90.03	87.8	2.23 (-3.31 to 7.78)	.81	.12
Physical Summary	44.46	53.0	-8.54 (-11.83 to -5.24)	-5.21***	.61
Psychosocial Summary	51.40	51.2	.20 (-2.48 to 2.87)	.15	.02

Note. *p <.05, **p < .01, ***p < .001.

Table 5.

Adolescent Report of Health-Related Quality of Life from Time 1 to Time 2.

Health-Related Quality of Life Domain	Time 2 Mean	Time 1 Mean	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*	*Pearson r*
Physical Functioning	93.06	91.90	1.16 (-2.12 to 4.43)	.71	.10	.45**
Bodily Pain	77.71	80.00	-2.29 (-9.05 to 4.46)	-.68	.10	.49**
Behavior	74.49	78.71	-4.23 (-9.08 to .63)	-1.75	.25	.36*
Mental Health	74.97	76.75	-1.79 (-5.42 to 1.84)	-.99	.14	.56***
Self-Esteem	83.05	81.22	1.83 (-1.22 to 4.87)	1.21	.17	.70***
General Health Perceptions	55.63	59.64	-4.01 (-7.60 to -.42)	-2.25*	.31	.61***
Family Activities	78.13	79.43	-1.30 (-7.00 to 4.40)	-.46	.07	.38**
Family Cohesion	74.58	71.67	2.92 (-6.59 to 12.42)	.62	.09	.15

Note. *p <.05, **p < .01, ***p < .001.

Table 6.

Parent Report of Health-Related Quality of Life from Time 1 to Time 2.

Health-Related Quality of Life Domain	Time 2 Mean	Time 1 Mean	Mean Difference (95% Confidence Interval)	*t*	*Effect size r*	*Pearson r*
Physical Functioning	85.53	89.58	-4.05 (-9.95 to 1.85)	-1.38	.20	.52***
Bodily Pain	76.46	79.58	-3.13 (-12.54 to 6.29)	-.67	.10	.25
Behavior	78.73	75.31	3.42 (-.16 to 7.00)	1.92	.27	.64***
Mental Health	74.14	76.04	-1.90 (-6.06 to 2.25)	-.92	.13	.60***
Self-Esteem	73.92	74.97	-1.04 (-6.44 to 4.36)	-.39	.06	.53***
General Health Perceptions	46.32	50.38	-4.06 (-7.68 to -.44)	-2.26*	.31	.71***
Family Activities	80.64	79.86	.78 (-6.98 to 8.54)	.20	.03	.11
Family Cohesion	82.40	79.69	2.71 (-3.06 to 8.48)	.95	.14	.60***
Role/Social - Physical	85.76	92.01	-6.25 (-15.16 to 2.26)	-1.41	.20	.03
Role/Social - Emotional/Behavioral	94.44	92.59	1.85 (-4.58 to 8.28)	.58	.08	.17
Parental Impact - Emotional	69.27	58.65	10.63 (1.74 to 19.51)	2.40*	.33	.34*
Parental Impact - Time	90.03	88.92	1.11 (-3.76 to 5.98)	.46	.07	.55***
Physical Summary	44.46	47.30	-2.84 (-6.20 to .52)	-1.70	.24	.45**
Psychosocial Summary	51.40	49.40	2.00 (-.03 to 4.03)	1.98	.28	.67***

Note. *p <.05, **p < .01, ***p < .001.

Table 7.

Correlations between Medical and Family Factors and Adolescent Report of Time 2 HRQOL.

		Adolescent-Reported Outcomes		
Adolescent-Reported Predictors	*n*	Time 2 Physical Functioning	Time 2 Mental Health	Time 2 General Health Perceptions
Time 1 Conflict	48	-.07	-.26	-.27
Time 1 Cohesion	48	.01	.25	.20
Time 1 % Adherence	47	-.17	-.28	.02
Time 1 Side Effects	48	-.39**	-.35*	-.34*
Time 1 Tacro SD range	36	-.21	-.34*	-.39
Time 2 Conflict	48	-.07	-.38**	-.38**
Time 2 Cohesion	48	.25	.38**	.19
Time 2 % Adherence	47	.34*	.40*	.44**
Time 2 Side Effects	48	-.24	-.65**	-.49**
Time 2 Tacro SD range	33	.06	-.20	.03
Hospitalizations Since Time 1	42	-.43**	.01	-.12
Rejections Present Since Time 1	43	-.05	-.17	-.21

Note. *$p < .05$, **$p < .01$.

Table 8.

Correlations between Medical and Family Factors and Parent Report of Time 2 HRQOL.

		Parent-Reported Outcomes		
Parent-Reported Predictors	*n*	Time 2 Physical Functioning	Time 2 Mental Health	Time 2 General Health Perceptions
Time 1 Conflict	48	.01	-.27	-.04
Time 1 Cohesion	48	-.05	.16	.05
Time 1 % Adherence	45	-.14	.04	-.22
Time 1 Side Effects	48	-.07	-.35*	-.33*
Time 1 Tacro SD range	36	-.04	-.11	-.03
Time 2 Conflict	48	.10	-.36*	.05
Time 2 Cohesion	48	.01	.37*	-.12
Time 2 Adolescent-Parent Relationship Domain	46	-.24	-.45**	.00
Time 2 % Adherence	47	.04	.23	-.21
Time 2 Side Effects	48	-.43**	-.65**	-.50**
Time 2 Tacro SD range	33	-.27	-.19	-.23
Hospitalizations Since Time 1	42	-.53**	-.01	-.35*
Rejections Present Since Time 1	43	-.19	-.18	-.14

Note. *$p < .05$, **$p < .01$.

Table 9.

Hierarchical Regression Predicting Time 2 Adolescents' HRQOL Physical Functioning.

Variable	***B***	***SE B***	***β***
Adolescent Report			
Step 1:			
Income	1.71	0.71	.32*
Time 1 Physical Functioning	0.36	0.11	.43**
Step 2:			
Income	1.54	0.59	.29*
Time 1 Physical Functioning	0.42	0.10	.50**
Hospitalizations since Time 1	-4.02	0.95	-.48**
Parent Report			
Step 1:			
Time 1 Physical Functioning	0.72	0.16	.58**
Step 2:			
Time 1 Physical Functioning	0.60	0.15	.48**
Hospitalizations since Time 1	-7.85	2.20	-.42**

Note. For adolescent report, R^2 = .31 for Step 1; ΔR^2 = .23 for Step 2 (*p*s < .01).

For parent report, R^2 = .34 for Step 1; ΔR^2 = .16 for Step 2 (*p*s < .01).

*p <.05, **p < .01.

Table 10.

Hierarchical Regression Predicting Time 2 Adolescents' HRQOL Mental Health.

Variable	*B*	*SE B*	*β*
Adolescent Report			
Step 1:			
Time 1 Mental Health	0.58	0.17	.50**
Step 2:			
Time 1 Mental Health	0.29	0.14	.26*
Time 1 Tacro SD range	-9.26	3.52	-.30*
Time 2 Side Effects	-0.44	0.11	-.53**
Parent Report			
Step 1:			
Time 1 Mental Health	0.72	0.14	.60**
Step 2:			
Time 1 Mental Health	0.50	0.14	.42**
Time 2 Family Cohesion	3.56	1.47	.25*
Time 2 Side Effects	-0.38	0.12	-.38**

Note. For adolescent report, R^2 = .25 for Step 1; ΔR^2 = .36 for Step 2 (ps < .01).

For parent report, R^2 = .36 for Step 1; ΔR^2 = .23 for Step 2 (ps < .01).

*p <.05, **p < .01.

Table 11.

Hierarchical Regression Predicting Time 2 Adolescents' HRQOL General Health Perceptions.

Variable	*B*	*SE B*	*β*
Adolescent Report			
Step 1:			
Time 1 General Health Perceptions	0.69	0.13	.61**
Step 2:			
Time 1 General Health Perceptions	0.59	0.12	.52**
Time 2 % Adherence	0.77	0.25	.34**
Parent Report			
Step 1:			
Income	-2.34	0.90	-.26*
Time 1 General Health Perceptions	0.77	0.11	.68**
Step 2:			
Income	-2.24	0.88	-.24*
Time 1 General Health Perceptions	0.66	0.13	.58**
Time 2 Side Effects	-.20	0.11	$-.19^{+}$

Note. For adolescent report, $R^2 = .38$ for Step 1; $\Delta R^2 = .11$ for Step 2 ($ps < .01$).

For parent report, $R^2 = .58$ for Step 1; $\Delta R^2 = .03$ for Step 2 ($ps < .01$).

*$p < .05$, **$p < .01$, $^{+}$ $p < .10$.

CHAPTER 4

DISCUSSION

The present study examined health-related quality of life (HRQOL) in adolescent transplant recipients from an initial assessment to 17-months (on average) later. Results indicated that parent and adolescent reports of HRQOL were generally consistent at both times of assessment, as evidenced by significant intraclass correlations for all domains except Family Cohesion (at Time 1 and Time 2) and Bodily Pain (at Time 2 only). This finding did not support our hypothesis based on previous research which suggested that parents and children showed better agreement for domains that included observable behavior, such as physical functioning, versus domains that included non-observable behavior, such as self-esteem (Eiser & Morse, 2001a).

Despite their agreement, further analyses showed that there were significant mean differences in parent versus adolescent reports of HRQOL at both assessment periods. Specifically, adolescents endorsed more positive functioning on average in the domains of Self-Esteem and General Health Perceptions compared to their parents at both time periods. They also rated their Physical Functioning at Time 2 as better compared to their parents. Thus, adolescents tended to perceive their health-related quality of life as higher than their parents perceived it. This finding is consistent with our hypotheses and previous studies (Levi & Drotar, 1999; Parsons et al., 1999; Sundaram et al., 2007). It is unclear whether adolescents are overly positive, parents are more attentive to signs of illness or dysfunction, or some other factor accounts for these parent-adolescent differences.

Examination of parent report of HRQOL compared to the healthy normative sample for the CHQ-PF50 revealed that parents of adolescent transplant recipients reported lower physical functioning, worse general health perceptions, and more restrictions on family activities due to their child's health, consistent with our hypotheses. Parent report on the Physical Summary, but not Psychosocial Summary, was significantly lower than the normative sample. Parent report of adolescents' self-esteem was significantly lower than norms at Time 1, but not significantly different from norms at Time 2. Parents also reported significantly more negative emotional impact on themselves due to their child's health. These results were consistent with other studies who found lower report of functioning for General Health Perceptions, Parent Impact - Emotional, Family Activities, and Physical Summary but not Psychosocial Summary (Alonso et al., 2003; Sundaram et al., 2007). The results are contrary to other studies that found lower Psychosocial Summary scores reported by parents of adolescent transplant recipients (Bucuvalas et al., 2003; Fredericks et al., 2007).

On a positive note, parents reported significantly higher family cohesion compared to norms at both time periods. In other studies, family cohesion has not been reported to be significantly different from norms (Bucuvalas et al., 2003; Fredericks et al., 2007). Although parent and adolescent reports of family cohesion were not significantly correlated, parental report above the norm suggests a possible resiliency factor for these families.

On average, health-related quality of life domains seem to be relatively stable across time, as evidenced by few significant differences between Time 1 and Time 2 reports. However, adolescents reported a significant decrease in General Health Perceptions over time, as did parents. Follow-up hierarchical regression analyses showed that after controlling for Time 1 levels of General Health Perceptions, different medical factors were related to this change for

parents and adolescents. For parents, hospitalizations were important in assessing adolescents' general health. Hospitalizations are observable and may serve as indicators of health for parents, as well as reflect serious medical needs. For adolescents, percent adherence was predictive. Adherence is a behavioral factor, and poor adherence has been linked with negative physical outcomes (Falkenstein et al., 2004; Shemesh et al., 2004). This suggests that the relationship between health perceptions and adherence could be due to adherence leading to or maintaining positive physical outcomes or, conversely, nonadherence leading to poor physical outcomes. Although negative physical outcomes, such as hospitalizations and rejections, were not significant predictors, targeting adherence may be an avenue for increasing health perceptions.

An additional significant change from Time 1 to Time 2 was the improvement in Parent Impact – Emotional. It seems that parents were coping better with the impact of their adolescent's condition, despite the consensus perception that adolescents' general health condition had declined over time. This is an area worthy of further exploration.

Examination of correlates of Time 2 Physical Functioning showed that similar medical factors were significantly correlated for both adolescent and parent report. That is, more frequent side effects and more frequent hospitalizations were associated with poorer physical functioning. Additionally, adolescents' report of nonadherence was associated with poorer physical functioning. Regression analyses showed that Time 2 Physical Functioning was predicted by hospitalizations when Time 1 Physical Functioning was held constant for both adolescent and parent report. Given that frequency of hospitalizations can be utilized as a marker for physical health or severity of medical condition, this relationship would be expected.

Parent and adolescent reports of Time 2 Mental Health were associated with a variety of medical and family factors. In general, more frequent side effects, more family conflict, and less

family cohesion were associated with poorer mental health. For adolescents, out-of-range tacro levels (SD > 3) were negatively associated with mental health. For parents, poorer perceptions of the quality of their relationship with their adolescents were also negatively associated with mental health. Regression analyses showed that the medical factors of side effects and out-of-range tacro levels were significantly predictive of Time 2 Mental Health for adolescents, and the combination of side effects and family cohesion were significantly predictive for parents.

Together, these results indicate a dynamic relationship between medical factors, such as immunosuppressant level stability, and psychosocial factors, such as mental health. Of the two sets of variables, it is not surprising that medical factors would play a primary role in these adolescent transplant recipients' perceptions of HRQOL. However, although family factors were only predictive of parent-reported mental health in the regression models, family conflict was also correlated with health perceptions. In addition, medical adherence is an important behavioral factor that contributes to short-term and long-term health outcomes, and for adolescent report adherence was correlated with each of the three HRQOL domains assessed, including mental health. Further, in other studies, adherence has been associated with family cohesion and conflict (DiMatteo, 2004a; Fredericks et al., 2007; Simons et al., 2007). In conjunction with previous research, the current results suggest that targeting emotional and family functioning, as well as adherence behaviors, is likely to improve health-related quality of life for adolescent transplant recipients.

There were several limitations to this study. Despite relatively high re-enrollment for the follow-up period, the small sample size limited power to detect significant differences, particularly related to organ group. Additionally, more than half of the sample was comprised of kidney transplant recipients, and although no significant differences were noted across organ

group within this sample, the results may not generalize to all pediatric solid organ transplant recipients. Further, since there are guidelines for examining standard deviations of immunosuppressant drug assay levels for only one drug, tacrolimus (Shemesh et al., 2004), analyses utilizing these data were limited in sample size and power because some transplant recipients were prescribed other immunosuppressant medications. Additionally, the CHQ was used for adolescents who were older than the age range for which there is normative data. However, the use of the measure at both time periods allowed for longitudinal comparisons. Finally, multiple t-tests and regression analyses were conducted using a *p* value of .05. Although a Bonferroni correction was not used, the replication of the pattern of results from Time 1 to Time 2 and the consistency of results with other studies adds to the validity and generalizability of these results.

Future research in this area should continue to examine the contribution of a broader range of psychosocial factors and HRQOL, including coping behaviors, and parental, marital, and additional family factors. For example, examining family conflict and communication specific to medication adherence and healthcare, as opposed to general family conflict, may elucidate the relationships among these factors and HRQOL. Also, families should be followed over longer periods of time and earlier in the transplant process, including prior to and after first transplant, to more effectively assess HRQOL and medical outcomes for each group of organ recipients. Multi-site investigations would aid in these efforts. Finally, implementing evidence-based psychological interventions might improve family functioning and medical adherence, thus improving HRQOL and medical outcomes for this vulnerable population.

In conclusion, the results of this study suggested that several family and medical factors relate to various domains of HRQOL in adolescent transplant recipients. In particular, higher

family conflict, lower family cohesion, more difficult relationship between parent and adolescent, more frequent perceived side effects, and more frequent hospitalizations were related to poorer HRQOL. Health-related quality of life appeared to be relatively stable across a 17-month period; however, both adolescents and parents reported decreasing General Health Perceptions across that time. Interventions aimed to improve family cohesion and parent-adolescent relationships may help improve health perceptions.

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