The Relationship of Hope and Illness-Related Uncertainty to Emotional Adjustment and Adherence Among Pediatric Renal and Liver Transplant Recipients

Julie M. Maikranz,1 PhD, Ric G. Steele,1 PhD, ABPP, Meredith L. Dreyer,1 PhD, Aaron C. Stratman,1 PhD, and James A. Bovaird,2 PhD

1Clinical Child Psychology Program, University of Kansas, Lawrence, KS, USA and 2Department of Educational Psychology, University of Nebraska – Lincoln, Lincoln, NE, USA

Objective To examine, using partial least squares (PLS) modeling, the associations among hope, illness-related uncertainty, anxiety, depression, and adherence in a sample of children with renal and liver transplantsations. Methods Seventy pediatric renal and liver transplant recipients and their caregivers participated in a 3-month study which involved completing questionnaires and monitoring adherence via self-report and electronic monitoring (MEMSTM caps). A PLS estimation procedure was used to examine the associations among constructs in the theoretical model. Results Hope and uncertainty were associated with both depressive symptoms and anxiety, and depressive symptoms were associated with treatment adherence. The association of hope and adherence to treatment was fully mediated by depressive symptoms. Conclusions Findings suggest mechanisms for identifying patients that may be at risk for nonadherence and components for intervention programs to improve adherence rates among pediatric transplant recipients.

Key words adherence; anxiety; depressive symptoms; hope; pediatric transplantation; uncertainty.

Over the past three decades, major advances in organ transplantation have resulted in improved health outcomes and survival rates for pediatric transplant recipients. However, despite these advances, many children and adolescents who receive transplants remain at increased risk for complications and negative health outcomes. Post-transplant complications, such as opportunistic infections and graft rejections, occur among an estimated 27–66% of pediatric transplant recipients (Perlmutter, Vacanti, Donahoe, & Kleinman, 1985; Sokal, 1995). Although some of these complications are unavoidable, studies suggest that there is a strong correlation between nonadherence with the post-transplant medical regimen and the incidence of acute rejection, as well as loss of the transplanted organ (e.g., Falkenstein, Flynn, Kirkpatrick, Casa-Melley, & Dunn, 2004).

One factor that may increase the risk of nonadherence in chronic illness populations in general is the presence of significant symptoms of distress and decreased psychosocial functioning (e.g., van Srevellen, Chang, Garcia, & Lombardi, 2002). Despite vast differences in how individuals respond to chronic illness, some research suggests that youth with chronic illnesses are two to four times more likely than healthy controls to have a psychiatric diagnosis at some time during their childhood or adolescence (e.g., Garrison & McQuiston, 1989; Lavigne & Faier-Routman, 1992). Studies within child and adolescent populations confirm an association between such compromised emotional functioning and poorer treatment adherence (Lurie et al., 2000; Shaw, Palmer, Blasey, & Sarwal, 2003).

Results from a number of investigations suggest that uncertainty regarding medical conditions or treatments...
may be associated with increased psychosocial distress (e.g., Molassiotis, Callaghan, Twinn, & Lam, 2001). While most of the literature in this area has focused on adults, some studies have examined illness-related uncertainty among children who have a chronic illness (i.e., asthma and diabetes; Hoff, Mullins, Chaney, Hartman, & Hommel, 2001) and among children who have a chronically ill parent (Steele, Tripp, Kochick, Summers, & Forehand, 1997). Overall, the literature suggests that illness-related uncertainty negatively impacts children’s emotional adjustment, regardless of who reports the uncertainty (i.e., parent or child) and regardless of who is ill (i.e., parent or child).

Beyond identifying emotional adjustment problems that are associated with nonadherence, it is therapeutically advantageous to promote good mental and physical health by focusing on children’s strengths that may be conducive to better medical adherence. During the past few decades, psychologists and health professionals have become increasingly interested in the correlates and consequences of hope, one of the most critical aspects of the positive psychology movement. Snyder, Irving, and Anderson (1991) have defined hope as “a positive motivational state that is based on an interactively derived sense of successful (a) agency (goal-directed energy) and (b) pathways (planning to meet goals)” (p. 287). Agency is the motivational component of hope and involves an individual’s belief in his or her ability to initiate and sustain the actions necessary to reach his or her goals and is characterized by self-statements such as “I know I can do this” and “I will finish this.” “Pathways thinking” involves an individual’s belief in his or her ability to produce one or more effective paths to his or her desired goals and is characterized by self-statements such as “I’ll find a way to get this done.”

Snyder and colleagues (Synder et al., 1997) have hypothesized that when high-hope people become physically ill, their effective goal-directed thinking enables them to stay appropriately aroused and focused on what they need to do to recuperate. In fact, a few existing studies suggest that high hope is associated with improved adherence among adult populations (Seaton & Snyder, 2001; van Servellen et al., 2002). Unfortunately, to date, only one study has been identified that examined the associations between hope and emotional adjustment in children with chronic illness. In an investigation of children with sickle cell disease, Lewis and Kliewer (1996) reported that higher levels of self-reported hope predicted the increased use of active coping strategies, which, in turn, predicted positive outcomes (i.e., less anxiety).

The purpose of the present investigation was to examine hope and uncertainty and their associations to psychosocial adjustment and adherence among children who have received renal or liver transplants. To this end, the present investigation made use of partial least squares estimation (PLS; Falk & Miller, 1992; Wold, 1980) to test a model of the association of hope and uncertainty to child psychosocial adjustment in a large sample (n = 70) of children that had received transplants. Consistent with previous literature, both hope and uncertainty were hypothesized to be directly associated with child psychosocial adjustment, and child psychosocial adjustment was hypothesized to be directly associated with adherence. Specifically, it was hypothesized that pediatric transplant patients and their parents who reported higher levels of hope would evidence better adherence to the child’s medication regimen. Similarly, it was hypothesized that pediatric transplant patients and their parents who reported low levels of illness-related uncertainty would evidence better adherence to their medication regimen. However, for both hope and illness-related uncertainty, it was hypothesized that the child’s emotional adjustment would mediate the hypothesized relationships, such that high levels of hope and low levels of uncertainty would predict better psychological adjustment (i.e., lower depressive and anxious symptoms), which would in turn, predict better medical adherence.

**Method**

**Participants**

The participants for the current project were drawn from a sample of 157 eligible families who were receiving post-transplant care from the renal and liver transplant teams at five children’s hospitals across the Midwestern United States between May 1, 2002 and November 30, 2004. Eligibility criteria for study entry included (a) that the child was a renal or liver transplant recipient, (b) between the ages of 7 and 18 years, (c) at least 6 months post-transplant, (d) the family was English-speaking, and (e) their legal guardian provided informed consent for the child to participate. Data were not collected from children under the age of 7 years or from patients with a documented developmental delay (i.e., standard IQ obtained within the calendar year that was less than 65) because child self-report data were necessary to test the hypotheses of the present study.
Of the 157 eligible families at the five hospitals, a total of 75 families agreed to participate in the study. This reflects an overall participation rate of 48% and an average participation rate across the five hospitals of 79.8%.¹ Five of the families who agreed to participate in the study were excluded from the present analyses because they failed to complete the questionnaires. Thus, a total of 42 liver transplant recipients and 28 renal transplant recipients and one of their primary caregivers, generally the biological mother (60 mothers, 8 fathers, 1 stepmother, and 1 grandmother). The participants ranged from 7 to 18 years of age (M = 13.32, SD = 3.22) and approximately half were boys (51.4%). A detailed summary of demographic information for the 70 participating families is presented in Table I.

**Procedure**

All participants who met eligibility criteria and were interested in participation met with the study personnel to discuss the project and provide informed consent (or, for children, assent). At this initial interview, caregivers and children were asked to complete a series of paper and pencil measures (see later). If multiple caregivers accompanied the child to the appointment, the caregiver who reported being most responsible for the child’s healthcare and medication regimen was asked to complete the questionnaires. The questionnaires were read to all children unless their primary caregiver indicated that the child was able to complete the questionnaires independently. Adolescents and parents were given oral directions and were asked to complete the questionnaires on their own unless they requested additional assistance.

Information on the children’s adherence to their post-transplant treatment regimens was collected via subjective measures (i.e., interviews) and objective data (Medication Events Monitoring System; MEMs™). Families who completed measures at the initial assessment were provided with a MEMs™ cap and were instructed on its proper use. Families were contacted by phone once each month during the 3 months following the visit to re-administer the interview for adolescent or caregiver-reported child adherence.

**Measures**

**Demographics**

Demographic data were obtained from the patients’ caregivers and include patient’s age and gender, caregiver’s age, time since transplant, number of transplants received, ethnicity, monthly income, caregiver’s educational level and marital status, and family composition.

**Hope (Parent and Child Measures)**

The Adult Trait Hope Scale (ATHS; Snyder et al., 1991) is a self-report measure that taps dispositional hope in persons aged 15 and older. The ATHS consists of 12 items: four agency, four pathways, and four distractor items. “I energetically pursue my goals” is an example of an agency item and “I can think of many ways to get out of a jam” is an example of a pathway item. Previous research has indicated excellent internal consistency, test–retest reliability, and construct validity (Snyder et al., 1991; Babyak, Snyder, & Yoshinobu, 1993). Ratings of internal consistency

| Table I. Demographic Characteristics of Participants in the Study Sample |
|----------------|---------------------------|--------------------------|
| Variable       | Mean (SD)                 | Frequency (%)            |
| Age of child   | 13.32 (3.22)              |                          |
| Time since most recent transplant | 5.97 (4.13)           |                          |
| Ethnicity      |                           |                          |
| Caucasian      | 80.0                      |                          |
| African American | 11.4                    |                          |
| Other          | 8.5                       |                          |
| Marital status |                           |                          |
| Married        | 77.1                      |                          |
| Divorced       | 17.1                      |                          |
| Single or widowed | 5.7                     |                          |
| Education level of mother/father |             |                          |
| Did not graduate from high school | 7.1/6.2              |                          |
| Graduated from high school | 31.4/38.5            |                          |
| Some college   | 32.9/20.0                 |                          |
| Graduated from college | 25.7/21.5          |                          |
| Graduate degree | 2.9/13.8                |                          |
| Monthly income |                           |                          |
| Less than $2000 | 23.3                     |                          |
| $2001–$4000 | 32.9                      |                          |
| $4001 and above | 28.5                   |                          |
| Missing        | 14.3                      |                          |
for the present project yielded a Cronbach's alpha coefficient of .90.

The Adult State Hope Scale (Snyder et al., 1996) differs from the Trait Hope Scale in that it taps ongoing goal-directed thoughts at a given moment in time. The measure has three pathway and three agency items on which respondents describe themselves in terms of how they are "right now." The scale has good internal reliability, and also demonstrates convergent and discriminant validity in terms of its relation to other state self-report indices (Snyder et al., 1996). The coefficient alpha for the present study was .90.

The Children's Hope Scale (CHS, Snyder et al., 1997) is a 6-item self-report measure that is used to assess trait hope in children aged from 7 to 16 years. The internal and test–retest reliabilities have been documented, as has the two factor structure of the scale (Snyder et al., 1997). Studies also support its convergent and discriminant validity in terms of yielding predicted relationships with other self-report scales for children (Snyder et al., 1997). The scale has been administered to both healthy children and those with a variety of medical problems such as cancer, asthma, and sickle-cell disease (Moon, Snyder, & Rapoff, 2001; Snyder et al., 1997). Demonstrated internal and temporal reliabilities are adequate (Snyder et al., 1997). To facilitate measurement equivalence, and because of the small anticipated number of 17-year-old and 18-year-old participants in the study, all child participants were administered the CHS. Cronbach's alpha for the present study was .81.

Illness-Related Uncertainty (Parent and Child Measures)

The Parent's Perception of Uncertainty in Illness Scale (PPUS, Mishel, 1983) is a self-report measure that assesses parents' uncertainty regarding their children's illnesses. The PPUS contains 31 items that tap four factors related to uncertainty: ambiguity, lack of clarity, lack of information, and unpredictability. The coefficient alphas for these factors range from .72 to .87 (Mishel, 1983). A score can be obtained for each factor and for the total PPUS. The analyses for the present study utilized the PPUS total score. For the current project, Cronbach's alpha for the overall scale was .85.

The Child Uncertainty in Illness Scale (CUIS, Mullins & Hartman, 1995) is a modified version of the 23-item Mishel Uncertainty in Illness Scale Community Form that has been adapted to be a developmentally appropriate self-report measure of illness uncertainty for children and adolescents with chronic illness. Previous investigations (e.g., Hoff, Mullins, Chaney, Hartman, & Domek, 2002) have indicated good internal consistency (α = .89). Ratings of internal consistency for the present project yielded a Cronbach’s alpha coefficient of .86.

Psychological Functioning (Parent and Child Measures)

The Behavioral Assessment Scale for Children, Parent Report Form (BASC-PRF, Reynolds & Kamphaus, 1992) is a comprehensive measure of numerous aspects of a child's adaptive and problem behaviors in community and home settings. Two forms of the PRF were used for this study: child (6–11 years) and adolescent (12–18 years). Parents were given the form that corresponded to the age of their child. This measure has demonstrated good internal consistency and test–retest reliability (Reynolds & Kamphaus, 1992).

The Behavioral Assessment Scale for Children, Self-Report of Personality (BASC-SRP, Reynolds & Kamphaus, 1992) is a measure of children's own perception of their behavior and feelings. The SRP has forms at two age levels: child (6–11 years) and adolescent (12–18 years). Participants were given the form that corresponded to their age. This measure has demonstrated good internal consistency and test–retest reliability (Reynolds & Kamphaus, 1992).

The Children's Depression Inventory (CDI, Kovacs, 1992) is a 27-item self-rated symptom oriented scale that provides a total score for depressive symptoms and several subscales including mood disturbance, self-perceptions, and relationships with others. The CDI has well-established internal consistency and validity (Kovacs, 1992). The coefficient alpha for the present study was .83.

State-Trait Anxiety Inventory for Children (STAIC; Spielberger, Edwards, Montuori, Lushene, & Platzeck, 1970) is comprised of separate, self-report scales measuring two distinct anxiety concepts: state anxiety (S-Anxiety) and trait anxiety (T-Anxiety). Although the STAIC was constructed to measure anxiety in nine-to twelve-year old children, the STAIC may also be used with younger children with average or above average reading ability and with older children. Reported T-anxiety alpha coefficients were .79 or greater with a median alpha of .88 for the sample of kindergartners, first graders, and second graders that were tested (Spielberger et al., 1970). Similarly, reported S-anxiety alpha coefficients ranged between .71 and .76 during individual testing (Spielberger et al., 1970). Again, to facilitate measurement equivalence, all child participants (ages 7 through 18 years) were administered the
STAIC scales. The T-anxiety and S-Anxiety alpha coefficients for the present study were .90 and .87, respectively.

Adherence
The current study used both subjective and objective measures of adherence. First, adolescent or caregiver self-report of child adherence (SRA) was obtained via a semi-structured interview developed for the present study based on interview questions recommended by Hecht and Davis (1998). Depending on who reported taking primary responsibility for medication dosing, caregivers or adolescents were asked by the researchers to identify each prescribed medication and the number of daily doses prescribed. Then, participants were asked to report the number of doses of the main immunosuppressant medication that were missed over the previous 3 days. SRA was calculated as the percent of prescribed doses that were successfully administered for each medication (e.g., number of doses administered divided by doses prescribed). The semi-structured interview was completed once during the initial interview, and again by phone each month during the 3 months following the clinic visit. When conducting the phone interviews, the researchers spoke with either the parent or adolescent when indicated. The three monthly SRAs obtained were averaged to arrive at the overall value used in the analyses.

Adherence was also measured via the MEMSTM data. The MEMSTM involves an ordinary medication bottle and a specially designed cap that includes a microchip. This microchip records bottle openings and keeps the data until the patient mails his or her pill bottle back to the researchers’ office where the dosing information can be downloaded. MEMSTM caps have been used successfully in both the adult and the pediatric patients to measure adherence (e.g., Gerson, Furth, Neu, & Fivush, 2004). This type of measurement provides dosage information for all of the time between physician appointments. Adherence as assessed by MEMSTM was calculated as the number of recorded doses divided by the number of prescribed doses over the 3-month study period.

Results
Overview of Analyses
Missing Data
Overall, 94% of the dataset was complete. However, for the overall project, MEMSTM cap data were missing for 40% of participants (n = 28). The majority of the missing MEMSTM data resulted from participants failing to return their MEMSTM cap (n = 18). Additional MEMSTM data were lost because of early return (n = 3), misuse (n = 2), lack of use (n = 2), post office personnel interference (n = 1), lost in the mail (n = 1), and battery failure (n = 1).

There is no direct mechanism for handling incomplete observations within the PLS framework, so multiple imputation was used to obtain a dataset with complete cases. Multiple imputation has been recommended as a method for handling missing data due to its ability to use information within the entire dataset when creating an algorithm for statistically calculating likely approximations of unobserved values (Schafer & Graham, 2002; Wayman, 2003). All variables of relevance to the study itself, all child demographic information, and all other variables that are not functions of other variables in the dataset were used with SAS PROC MI to create five parallel datasets with complete observations for all cases. Each dataset was analyzed separately, and resulting parameter estimates were combined using Rubin’s (Little & Rubin, 1987) rules for combining estimates. All parameter estimates reported and discussed are combined estimates.

Standard Errors
In the PLS framework, standard errors are obtained through a nonparametric resampling procedure called bootstrapping (Efron & Tibshirani, 1993). In short, bootstrapping involves repeated random sampling with replacement from the original obtained sample to create a bootstrap sample. The proposed model is then fit to this bootstrap sample, model parameters are estimated, and the process is repeated. The repeated bootstrap parameter estimates are used to create an empirical sampling distribution for each model parameter, and the standard deviation of the empirical sampling distribution is the empirical standard error for the parameter. The parameter estimate from the original sample divided by the empirical standard error is then used as a t-statistic for parameter inference. Empirical standard errors were obtained through 1,000 bootstrap samples, and this process was repeated for each of the five multiple imputation datasets.

2The empirical standard errors obtained through bootstrapping are in contrast to normal-theory standard errors obtained in traditional methods. PLS does not rely on any normality-related assumptions, thus normal-theory standard errors are not available.
Partial Least Squares Analysis

A partial least squares estimation procedure was used to examine the hypothesized relationships between constructs depicted in the theoretical model (Chin, 2001). Similar to structural equation modeling, PLS can be used to accomplish the combined tasks of factor analysis and multiple regression in order to maximize the predictive relationship between variables within a given dataset. However, structural equation modeling relies on maximum likelihood estimation, which requires a larger sample size than what was available given the current population of interest. Within PLS, the relationship between a set of manifest variables (e.g., SRA, MEMS) and their hypothesized constructs (e.g., “adherence”) are assessed. In PLS, having multiple measures of the constructs allows for the disattenuation of modeled relationships for the unreliability of the individual measures. Thus, the more observed variables that a particular latent construct has, the more likely that latent construct identifies what it represents, according to measurement theory. These “outer model” estimates are expressed as loadings or weights for each indicator (Figure 1), and specify how well each indicator relates to the latent construct. The inner model (i.e., associations among latent variables) is then obtained by regression coefficients that simultaneously describe the linear relationships between the constructs. The program PLS-Graph (Chin, 2001) was used for all PLS analyses.

Figure 1. Full model of direct and indirect associations of hope and uncertainty to adherence, depressive symptoms, and anxiety. Significant associations between latent constructs are presented in bold face. ASHS, Adult State Hope Scale; ATHS, Adult Trait Hope Scale; CHS, Children’s Hope Scale; UNC, Uncertainty Latent variable; PPUS, Parent’s Perception of Uncertainty in Illness Scale; CUIS, Children’s Uncertainty in Illness Scale; DEP, Depressive symptoms latent variable; BASC-PRF, Behavioral Assessment Scale for Children-Parent Report Form; BASC-SRP, Behavioral Assessment Scale for Children-Self Report of Personality; CDI, Children’s Depression Inventory; ANX, Anxiety symptoms latent variable; STAIC-S, State-Trait Anxiety Inventory for Children, State Anxiety; STAIC-T, State-Trait Anxiety Inventory for Children, Trait Anxiety; ADH, Adherence Latent Variable; SRA, Self-reported adherence (from interview); MEMS, Medication Event Monitoring System; ‘p<.01.'
Preliminary Analyses

Means, standard deviations, and informants for the indicators are presented in Table II according to the latent variable to which they contributed. Preliminary correlational analyses were conducted to determine whether any additional demographic (i.e., gender and ethnicity; parent marital status; family income) or transplant-related (i.e., hospital site, type of organ, age at transplant, number of medications prescribed) variables were related to the study variables. Due to the large number of correlations being conducted, a Bonferroni-corrected criterion ($p = .05/224 = .0002$) was utilized when determining statistical significance. None of the correlations were significant at this level. Thus, demographic and transplant-related variables were not added to the model.

Test of the Model

The full model is presented in Figure 1. Overall, the model demonstrated a reasonable fit to the data (average $R^2 = .203$, average Communality = 0.528, and average redundancy = 0.141) and accounted for 15% of the variance in children’s adherence to post-transplant medications. In terms of specific associations between latent constructs, the significant pathways of the full model were between the latent variables Hope and Uncertainty ($B = .45, SE = .10, p < .01$), Hope and Depression ($B = .47, SE = .10, p < .01$), Uncertainty and Anxiety ($B = .38, SE = .10, p < .01$), Uncertainty and Depression ($B = .35, SE = .08, p < .01$), and Depression and Adherence ($B = -.57, SE = .23, p < .01$). On the other hand, pathways between the latent variables Anxiety and Adherence, Hope and Adherence, and Uncertainty and Adherence were not statistically significant.

Tests of Mediation

Rather than traditional multi-step regression-based methods of analyzing mediated relationships (e.g., Baron & Kenny, 1986), PLS allows for simultaneous testing of direct and indirect effects where the significance of indirect effects (i.e., the mediated relationship) is determined by calculating a $z$ score based on the product of the estimated path coefficients ($a' \times b'$), and the estimated standard errors are obtained by the

<table>
<thead>
<tr>
<th>Latent variable</th>
<th>Indicator</th>
<th>Informant</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertainty</td>
<td>PPUS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Caregiver</td>
<td>58.35 (13.19)</td>
<td>35–88</td>
</tr>
<tr>
<td></td>
<td>CUIS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>55.62 (14.26)</td>
<td>29–90</td>
</tr>
<tr>
<td>Hope</td>
<td>Adult State Hope Scale</td>
<td>Caregiver</td>
<td>37.90 (6.65)</td>
<td>18–48</td>
</tr>
<tr>
<td></td>
<td>Adult Trait Hope Scale</td>
<td>Caregiver</td>
<td>49.81 (9.61)</td>
<td>28–64</td>
</tr>
<tr>
<td></td>
<td>Children’s Hope Scale</td>
<td>Child/adolescent</td>
<td>27.32 (5.47)</td>
<td>14–36</td>
</tr>
<tr>
<td>Anxiety</td>
<td>BASC-PRF Anxiety Scale&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Caregiver</td>
<td>53.91 (12.70)</td>
<td>29–93</td>
</tr>
<tr>
<td></td>
<td>BASC-SRP Anxiety Scale&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>46.01 (8.31)</td>
<td>34–66</td>
</tr>
<tr>
<td></td>
<td>STAIC-State Anxiety&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>28.69 (5.51)</td>
<td>20–48</td>
</tr>
<tr>
<td></td>
<td>STAIC-Trait Anxiety&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>32.22 (8.78)</td>
<td>20–50</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>BASC-PRF Depression Scale&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Caregiver</td>
<td>51.33 (14.08)</td>
<td>34–108</td>
</tr>
<tr>
<td></td>
<td>BASC-SRP Depression Scale&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>47.33 (7.33)</td>
<td>41–80</td>
</tr>
<tr>
<td></td>
<td>CDIf&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Child/adolescent</td>
<td>44.34 (7.72)</td>
<td>34–65</td>
</tr>
<tr>
<td>Adherence</td>
<td>Self-report</td>
<td>Caregiver</td>
<td>97.46 (7.01)</td>
<td>5.8–100</td>
</tr>
<tr>
<td></td>
<td>MEMS&lt;sup&gt;g&lt;/sup&gt;</td>
<td>MEMSTM cap</td>
<td>69.17 (31.94)</td>
<td>66.5–100</td>
</tr>
</tbody>
</table>

<sup>a</sup>Parent’s Perception of Uncertainty in Illness Scale; <sup>b</sup>Children’s Uncertainty in Illness Scale; <sup>c</sup>Behavioral Assessment Scale for Children–Parent Report Form; <sup>d</sup>Behavioral Assessment Scale for Children-Self-Report of Personality; <sup>e</sup>State-Trait Anxiety Inventory for Children; <sup>f</sup>Children’s Depression Inventory; <sup>g</sup>Medication Event Monitoring System.
Sobel (1982) procedure. Tests of significance were calculated using Preacher and Leonardelli’s (2001) interactive calculation tool for mediation tests. Tests of the indirect effect showed full mediation of Hope through Depression to Adherence when controlling for Uncertainty and Anxiety ($z = 2.19, p < .05$). In addition, tests of the indirect effect showed full mediation of Uncertainty through Depression to Adherence when controlling for Hope and Anxiety ($z = -2.11, p < .05$).

**Discussion**

Published rates of nonadherence for pediatric renal and liver transplant recipients are alarmingly high and have led clinicians and researchers to stress the importance of discovering the specific factors that are associated with adherence. Identifying these factors is a necessary first step in determining which patients are at risk for nonadherence and to develop programs aimed at improving adherence (Lurie et al., 2000). In order to take this necessary first step, this investigation proposed that hope, illness-related uncertainty, anxiety, and depression are all factors that interact to predict adherence among pediatric renal and liver transplant patients.

In the full model, depressive symptoms fully mediated the relationship between hope and adherence and the relationship between illness-related uncertainty and adherence. As hypothesized, individuals with high levels of hope and low levels of illness-related uncertainty were likely to adhere to their medical regimen only to the extent that they were not experiencing symptoms of depression. On the other hand, anxiety did not appear to fully mediate the relationship between hope and adherence or the relationship between uncertainty and adherence.

Consistent with research conducted in other populations (e.g., Lewis & Kliwer, 1996) our results indicate that hope is associated with both anxiety and depression in families that have undergone pediatric transplant surgeries. Given that children’s depressive symptoms and anxiety are important endpoints in-and-of themselves, our results suggest one possible strategy for alleviating children’s distress. Cognitively based therapies to raise hope levels have received some support in the literature (see Lopez et al., 2004 for a review). Such interventions may be indicated for families impacted by organ transplant surgery.

Also consistent with prior findings (Hoff et al., 2001; Steele et al., 1997), lower illness-related uncertainty scores were related to lower anxiety scores and lower depression scores. Researchers have speculated that, “uncertainty becomes associated with aversive outcomes (e.g., poorer disease control) and subsequent increases in emotional distress” (Mullins, Chaney, Pace, & Hartman, 1997, p. 877). Of course, uncertainty is not always avoidable in illness situations where care decisions are based on the educated use of probabilities (Christman et al., 1988). As a result, determining the perceived level of illness-related uncertainty should be a useful clinical tool for determining a child’s risk for experiencing anxiety and/or depression. Recognizing that children and families vary on the degree to which they seek and adaptively use procedural or medical information (e.g., Rudolf, Denig, & Weisz, 1995), future prevention and intervention programs that focus on increasing the amount or clarity of information that families and children receive about the transplant procedure should be investigated. Our results suggest that such interventions may decrease post-transplant anxiety and depressive symptoms. However, prospective studies should be conducted to determine the generalizability of these associations.

The present study makes many unique contributions to the literature. First, this study investigated two variables—hope and illness-related uncertainty—that have not previously been examined in relation to adherence in the pediatric transplant literature. This research deficit exists even though hope has been significantly related to adherence within other pediatric illness populations (Moon et al., 2001). Second, the present study made use of a multiconstruct model to predict adherence. Pediatric transplant recipients and their families face numerous challenges related to the transplant process. Thus, it is unlikely that any one predictor of adherence would be identified as the sole influence. In the present study, the model of adherence incorporated multiple psychosocial factors and the interactions between those factors. Third, the present study offers an unusually large, geographically diverse sample to the literature on pediatric transplantation. The diversity of treatment sites may add to the generalizability of our findings. Finally, the present study employed multiple measures of adherence to ensure a more reliable and valid assessment of adherence. Currently, there are few published studies that use different methods to detect adherence of renal and liver transplant recipients.

Although this study has many strengths, it is not without limitations. First, the meditational hypotheses were evaluated based on cross-sectional instead of
longitudinal data. Thus, it was neither possible to infer directions of causality in the relationships among constructs, nor was it possible to examine the degree to which pre-transplant hope and uncertainty predicted post-transplant adjustment or adherence. Second, the study included participants who were 7 through 18 years old. Such an age range was necessary to accrue a sufficient sample for these analyses. However, given the wide range of physical, cognitive, developmental, and social differences that exist between children and adolescents, separate examinations of children and adolescents may be advantageous. This is especially true given that some participants fell outside of the indicated range of some study instruments.

Third, manifest variables from different reporters were combined to create latent constructs. As this was the first exploration of these constructs, it made theoretical sense to establish broad hope and illness-related uncertainty variables. However, inspection of the statistical composition of the hope and illness-related uncertainty variables suggested that data from parents and patients could be separated into distinct components. Given that child-reported hope and uncertainty contributed more variance to the PLS model than parent measures, it may be especially important for future studies to examine the unique contributions of parent and child variables in this population. Likewise, the relatively low factor loading of self-reported adherence on the adherence latent variable suggests the need for additional examination of adherence methods in this population.

Finally, although electronic monitoring may provide a more direct and objective measure of medication dosing, this method also has limitations. MEMSTM caps are subject to human (e.g., failure to use or return for analysis) and mechanical error (e.g., battery failure, loss of cap). The failure of a significant number of families to return MEMSTM caps were among the less adherent and perhaps more distressed patients/families in the sample. However, if this is the case, we might expect that the magnitude of our findings would have been enlarged by the inclusion of these potentially more distressed, less adherent families.

Clinically, this study provides several points for consideration. First, our results suggest the importance of including measures of hope, illness-related uncertainty, and depression as part of the pre-transplant evaluation as well as part of regular post-transplant evaluations. For patients and families who report low levels of hope, high levels of illness-related uncertainty, or high levels of depressive symptoms, mental health professionals are encouraged to work with the family toward developing strategies for increasing their hopeful thinking, decreasing their uncertainty regarding the illness experience, and improving their emotional adjustment (i.e., decreasing depressive symptoms).

Because illness-related uncertainty includes issues related to the medical treatment (e.g., “I don’t know why I have to do each of my treatments’’), as well as issues regarding individuals’ personal experiences (e.g., “I never know how I will feel, I have good days and bad days”), pre-transplant families or families of newly transplanted children might be paired with “mentor families” who are familiar and have had long-term success with the transplant process (Snyder, 1995). In addition, treatment teams are encouraged to “touch base” with families to assess uncertainty regarding medical procedures, side effects, or changes in status or prognosis on a regular basis over the course of post-transplant therapy. As noted earlier, prospective longitudinal investigations will be necessary to develop and evaluate the efficacy of treatments designed to reduce uncertainty in these families.

For post-transplant families with poor adherence, our results suggest that it may be useful to consider whether the adherence problem is related to a lack of motivational agency or depressed mood. Psychoeducational programs designed to alleviate depression and increase hopeful thinking should focus on increasing both components of hope (i.e., agency and pathway). Agency- and pathways-enhancing lessons might focus on strategies such as cognitive restructuring (i.e., encouraging families to think of adherence-related difficulties as challenges), specific problem solving strategies (see for example, Varni et al., 1999), and the use of positive self-statements to promote personal agency.

In summary, this study provides preliminary support for the notion that hope and illness-related uncertainty in the pediatric transplant population are indirectly associated with medical adherence through their direct association with depressive symptoms. This investigation suggested multiple points of intervention that could lead to increases in adherence rates. Further research into the role of hope, illness-related uncertainty, and depression in relation to adherence will aid in the continued development of effective treatment programs to counter
nonadherence in this population. Because depression was such a powerful mediating force, additional focus might be placed on the assessment and treatment of depression for pediatric transplant recipients.

Acknowledgements
This investigation was supported by University of Kansas General Research Fund allocation #2301132 awarded to Ric G. Steele, PhD. Data analysis was supported by a research grant from the NICHD (Mental Retardation Research Center Grant-HD02528). We thank the liver transplant staff at Children’s Mercy Hospital, Cardinal Glennon Children’s Hospital, St Louis Children’s Hospital, Cincinnati Children’s Hospital Medical Center, and Baptist Medical Center of Oklahoma. We are also grateful to the renal transplant staff at Cincinnati Children’s Hospital Medical Center and St Louis Children’s Hospital. Finally, the authors wish to thank the participants and their families who helped us better understand how to improve adherence and the health of transplant patients in the future.

Conflict of interest: None declared.

Received February 22, 2006; revisions received July 10, 2006 and October 27, 2006; accepted November 6, 2006

References


Seaton, K., & Snyder, C. R. (2001). *Hope and remaining in a treatment program for drug abuse*. Unpublished manuscript, Department of Psychology, University of Kansas, Lawrence, Kansas.


