

## ABSTRACT

Title of Dissertation: PARENT PSYCHOLOGICAL FUNCTIONING,  
ILLNESS SEVERITY, AND MEDICAL ADHERENCE  
IN PEDIATRIC HEART TRANSPLANTATION

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This study examined parental psychological functioning, illness severity, and medical adherence in parents of pediatric heart transplant patients. It was hypothesized that parental psychological distress would be associated with increased illness severity and medical non-adherence. Data were collected on 52 parents of pediatric heart transplant patients through the use of parent report questionnaires, cardiologist ratings, medication levels, and medical chart review. Results indicated that 19% of parents met DSM-IV clinical criteria for Post-Traumatic Stress Disorder. When compared with a normative adult population, the study population had significantly higher rates of general psychological distress. Furthermore, 38% of parents were non-adherent on at least one measure of medical adherence. Analyses examining the relationships among parental psychological distress, illness severity, and medical adherence did not identify any statistically significant associations; however, a medium effect size was found for the

relationship between global psychological distress and non-adherence. Study limitations and implications for future research are discussed.

PARENT PSYCHOLOGICAL FUNCTIONING, ILLNESS SEVERITY, AND  
MEDICAL ADHERENCE IN PEDIATRIC HEART TRANSPLANTATION

by

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To Gail Konhaus Walter, Ph.D.

A seventeen year old girl thanks you for shining a light  
on her potential and her strength when she could not see them for herself

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## CHAPTER I

### Introduction

Pediatric heart transplantation was first performed in 1968, but the introduction of cyclosporine as an immunosuppressant medication revolutionized the field in 1983 (Chinnock 2002). The survival rates of patients receiving transplants dramatically improved, leading to a rapid increase in heart transplant centers in the United States (Kirklin et al., 2002). Today, heart transplantation is the standard of care for children with end stage cardiac illness (DeMaso, Kelley, Bastardi, O'Brien, & Blume, 2004). After transplantation, children and their parents continue to experience a chronic illness requiring long-term immunosuppression and repeated medical visits for the continued threat of organ rejection. Within this context, transplantation has been described as “trading one illness (end stage heart disease) for another (post-transplant care).” With children living longer, there is increasing interest in understanding the impact of heart transplantation and post-transplant medical care on the psychological functioning of parents caring for children who have received heart transplants.

The course of the heart transplant process is protracted in nature, beginning with the diagnosis and decision-making stage, the weeks to months waiting period prior to surgery, transplantation and hospitalization, and the post-transplant medical care which lasts the remainder of the child's life (Chinnock, 2002). The intensity and duration of the care following transplantation can be challenging and stressful, even for the most highly functioning families. Patients and their caretakers face the necessity for lifelong adherence to immunosuppressive medication, frequent medical visits, and invasive cardiac procedures (e.g., cardiac biopsies via catheterizations) to prevent and manage

organ rejection. In addition, they face numerous potential adverse side effects including hypertension, renal insufficiency, coronary artery disease, infections, seizures, and lymphomas.

Todaro, Fennell, Sears, Rodriguez, and Roche (2000) noted that the long-term aspect of transplantation may create more stress than is typically encountered by patients and families who are reacting to a single corrective surgical event, such as open heart surgery. Parents of transplant recipients are subjected not only to a single stressful event (e.g., the transplant surgery) at a specific point in time, but to the “cumulative adversity” experienced over the lengthy course of both the transplant surgery and the post-transplant medical care (Alonzo, 2000). Research has demonstrated a general relationship between family functioning and child adjustment in this population, yet the specific reactions and emotional symptoms of parents warrants further study (DeMaso, Twente, Spratt, & O’Brien, 1995; DeMaso, Kelley, Bastardi, O’Brien, & Blume, 2004). However, there has been no systematic examination in the literature of the specific aspects of psychological functioning of parents facing pediatric heart transplantation and its subsequent care.

Studies of children with cancer, bone marrow transplantation, and diabetes report that posttraumatic stress disorder (PTSD) is present in a significant subset of parents (Kazak et al., 1997; Manne et al., 2002; Landolt et al., 2002). PTSD is defined as a cluster of symptoms that develop after encountering extreme trauma, such as threatened death or the threat of serious personal injury or loss (American Psychiatric Association, 1994). One may also develop PTSD through witnessing harm or threatened harm to another person as well as “learning that one’s child has a life-threatening disease” (American Psychiatric Association, 1994, p. 424). Individuals who qualify for a

diagnosis of PTSD respond to the traumatic event with feelings of helplessness and fear. They experience intrusive memories or dreams of the event. They often try to avoid all reminders of the event, as exposure to trauma-related stimuli often leads to significant psychological distress. The individual may evidence decreased interest in usual activities and show limited affect. Furthermore, they may have difficulty sleeping and have an exaggerated startle response. These symptoms often result in significant social, occupational, or interpersonal difficulties (American Psychiatric Association, 1994).

One can speculate that the intensity and duration of the heart transplantation process may predispose a parent to the development of PTSD or possibly sub-threshold PTSD symptoms. In cases where posttraumatic stress symptoms are significant, parents' ability to cope effectively with the multiple demands of this chronic illness, such as frequent appointments, hospitalizations, and complicated medical regimens, could be significantly compromised. Furthermore, it may be that increasing medical severity of the child's illness may further compromise parental coping abilities. In parents of pediatric heart transplant patients, posttraumatic stress symptoms might be expressed through their reactions and responses to their child's transplant and subsequent medical management. For instance, the common PTSD symptom of avoidance might manifest itself through missing appointments or forgetting to give the child's medication on time. Therefore, it stands to reason that posttraumatic stress symptoms might be associated with difficulties adhering to the prescribed post-transplant medical recommendations.

Adherence to the medical regimen is also an area of limited clinical understanding, despite its critical importance to patient survival. In fact, it has been called "the best documented but least understood health-related behavior" (Becker &

Maiman, 1975, p. 11). Adherence is defined as patient behaviors that are in alignment with medical advice (Thompson & Gustafson, 1996, Haynes, 1979). Poor adherence after transplantation is identified as a major source of multiple complications, including organ rejection and increased mortality. (Dew, Roth, Thompson, Kormos, & Griffin, 1996; Dew et al., 1999). It is estimated that poor adherence occurs in over half of chronic pediatric medical patients (Rapoff & Bernard, 1991).

Prior research has demonstrated that posttraumatic stress symptoms are associated with non-adherence to the medical regimen in children following liver transplant (Shemesh et al., 2000). Research has also indicated that family functioning variables, such as family stress (Foulkes, Boggs, Fennell, & Sibinski, 1993), family cohesion (Serrano-Ikkos, Lask, Whitehead, Rees, & Graham, 1999), and parent-child conflicts (Shaw, Palmer, Blasey, & Sarwal, 2003) are significantly related to non-adherence in pediatric medical populations. The potential role of parental posttraumatic stress in post-transplant adherence remains understudied.

This study will examine the relationship between parental psychological functioning and adherence to the medical regimen in pediatric heart transplant recipients. I hypothesize that parents of transplant recipients will report global psychological distress, posttraumatic distress symptoms, and stress related to parenting a child with a chronic medical condition. Using multiple indicators of medical adherence (parental report, cardiologist rating, and drug assay data), the study will assess the relationships among parental functioning, illness severity, and adherence.

## CHAPTER II

### Literature Review

In the following review, literature on cardiac illness and pediatric heart transplantation, parental functioning during a child's medical illness, parental posttraumatic stress disorder, and medical adherence will be covered.

#### *Medical Illness in Children*

For the purposes of this study, a brief overview of pediatric cardiac illness and heart transplantation will be conducted to provide adequate background regarding the study population.

#### *Pediatric Cardiac Illness*

Heart disease in children comes in many forms, with variations in severity, age of onset, and treatment options. DeMaso (2001) divided pediatric cardiac illness into the following five categories: left-to-right shunts, complex cyanotic lesions, obstructive heart lesions, acquired heart disease/cardiomyopathies, and arrhythmias.

Left-to-right shunt lesions involve holes between the right and left sides of the heart. As a result, a shunt is created in which the pressures on the left side are higher than those on the right side. Blood is then directed to the lungs and away from the body. Such lesions include atrial septal defects, ventricular septal defects, and patent ductus arteriosus (DeMaso, 2001).

Complex cyanotic lesions are also known as "right-to-left shunt lesions." These lesions in the heart cause blood to be shunted toward the body and away from the lungs, resulting in decreased oxygen flow. Complex cyanotic lesions include tetralogy of fallot, transposition of the great arteries, truncus arteriosus, total anomalous pulmonary venous

return, tricuspid atresia, Ebstein's anomaly, single ventricle physiology, and double outlet right ventricle. These lesions are considered more severe than left-to-right shunt lesions and frequently require intensive medical intervention (DeMaso, 2001).

Obstructive lesions involve obstructions to the body's blood flow to the left or right sides of the heart. These lesions include mitral valve disease, left outflow defects, coarctation of the aorta, and aortic valve stenosis (DeMaso, 2001). Acquired heart diseases/cardiomyopathies represent an illness of the heart that the child acquires through either bacterial or viral infection or autoimmune dysfunction. The heart muscle does not pump effectively, and thus the body does not receive adequate oxygen.

Cardiomyopathies often result in arrhythmias and place the child at risk for sudden death. Acquired heart diseases include myocarditis (inflammation of the heart) and dilated cardiomyopathy (enlarged heart) (DeMaso, 2001). Finally, arrhythmias occur when the heart beats irregularly due to dysfunction in the heart's electrical conduction system. They are typically bradyarrhythmias, involving slow heart rate, or tachyarrhythmias, involving fast heart rate (DeMaso, 2001).

Cardiac illness in children may produce a variety of symptoms, including fatigue, shortness of breath, reduced exercise tolerance, and chest pain. Medical interventions include chest radiographs (x-rays), echocardiograms (ultrasound of the heart), electrocardiogram (test of electrical activity of the heart), cardiac catheterization (tissue sample is taken from the heart for evaluation), corrective surgery, medications designed to aid heart function, and heart transplantation (DeMaso, 2001).



### *Pediatric Heart Transplantation*

Pediatric heart transplantation is the current standard of care for children with end stage cardiac disease (Todaro et al., 2000). While it does not represent a “cure,” heart transplant is typically viewed as a life-prolonging or palliative procedure that generally occurs when the life expectancy of a child is less than one or two years (Fricker et al., 1999). In the United States, approximately 260 heart transplants are performed on children each year (Blume, 2003; Boucek et al, 2002). There is an 85% survival rate one year post-transplant, a 75% survival rate five years post-transplant, and a 65% survival rate ten years post-transplant (Boucek et al., 2002).

The greatest risks post-transplantation are infection and chronic rejection of the transplanted heart. The donated organ represents a foreign body to the recipient’s immune system, which subsequently produces an immune response to “attack” the new heart. Therefore, patients are given high doses of immunosuppressive medications, such as cyclosporine and tacrolimus, which help the body to accept the transplanted organ. Immunosuppressive therapy remains a life-long treatment in pediatric heart transplantation. Unfortunately, immunosuppressive drugs, while necessary, also weaken the immune system, thus increasing susceptibility to infections and malignancies (Blume, 2003).

Children may show the following symptoms when experiencing acute or chronic organ rejection: fatigue, decreased appetite, nausea, abdominal pain, rapid increase in weight, tachycardia, irregular rhythm, fever, hepatomegaly, ectopy, syncope (fainting), intermittent edema, exercise intolerance, and chest pain (Blume, 2003). There are multiple side effects that result from post-transplant medications, including moon facies

(fatty deposits that develop in the face, causing a round looking or “moon face” appearance), obesity, acne, facial hair growth, pubertal stage delay, and excessive gum growth (DeMaso, 2001).

There is relatively little research on the psychological functioning of children and families post heart transplantation. However, available research suggests that children generally demonstrate good psychological adjustment, although approximately 20%-24% of pediatric heart transplant patients evidence psychological distress (DeMaso, Twente, Spratt, & O’Brien, 1995; DeMaso, Kelley, Bastardi, O’Brien, & Blume, 2004; Todaro et al., 2000).

One study examined children’s psychological functioning both prior to and after heart transplantation (DeMaso et al., 1995). The sample consisted of 23 children and adolescents (13 females and 10 males) who were at least one-year post heart transplant. Measures included a global index of psychological functioning, measures of medical severity, and a global family functioning scale. Researchers found that most children (78%) exhibited positive psychological adjustment after heart transplant (DeMaso et al., 1995). There was no difference in the psychological functioning of children with congenital heart disease and children with acquired heart disease. Lower number of post-transplant hospitalizations was associated with levels of both pre and post-transplant psychological adjustment. Perhaps the most interesting finding was the correlation between family functioning and children’s psychological adjustment. Families with positive relational functioning were more likely to have children who were well adjusted both pre and post heart transplant. One major limitation of the study was the sample size.

However, given the relative low frequency of pediatric heart transplants, this study lends insight into future avenues of study (DeMaso et al., 1995).

### *Parental Functioning in Pediatric Medical Illness*

The diagnosis of a life-threatening medical illness in a child can generate profound fear, distress, and apprehension in parents. In addition to the usual concerns and responsibilities of raising a child, parents must face the difficult task of learning about the illness, possible treatments, and medication side effects. They encounter the challenge of explaining the illness to the child and his or her siblings in a developmentally appropriate and sensitive way. The illness often requires one or both parents to alter their work schedules to accommodate a potentially rigorous and time intensive treatment schedule. Additionally, parents must cope with the host of emotions that are ignited by learning news of a child's life-threatening illness. Although many parents and families adapt remarkably well, coping with severe pediatric illness often results in significant adjustment difficulties for some parents and families. Therefore, the literature on parental adjustment in a variety of pediatric illnesses will be outlined to document the current state of research on the psychological difficulties often experienced by this population.

### *Psychological adjustment of parents of children with cancer*

Kupst et al. (1995) examined pediatric leukemia patients and their families 10 years post-treatment. The sample consisted of 28 patients, 23 mothers, and 12 fathers who completed questionnaires related to adjustment, coping, and psychological symptoms. They found that, in general, most families coped well with the multitude of

stresses associated with cancer treatment and the necessary follow-up care. However, some families demonstrated higher levels of discord and maladjustment.

Kupst et al. (1995) found that low SES, young age at diagnosis, lack of social support, parental adjustment, and poor communication were related to difficulties in the family 10 years after the child's treatment for cancer. Importantly, the most significant predictor of child adjustment was maternal adjustment. The reverse relationship was also true, in that mother's coping was predicted by child adjustment. This study highlights the importance of the family when treating a medically ill child and the necessity of further research to help explain how parents and families are impacted by a life threatening illness (Kupst et al., 1995). A limitation of the study was the small sample size. Almost half of the original sample died within six years, and seven patients did not participate in the follow-up sessions. Additionally, the study did not have a control group.

In a study of 42 couples of children with cancer, researchers speculated that the marital relationship might be influenced by the intensity and chronicity of the disease (Dahlquist, Czyzewski, & Jones, 1996). They examined coping style, psychological distress, and marital adjustment at two time points: two months after learning of their child's cancer diagnosis and 20 months post-diagnosis. Correlational and multiple regression analyses revealed gender differences in emotional distress. Specifically, mothers were significantly more anxious than fathers two months post-diagnosis. While mothers' anxiety dropped at the 20-month follow-up, fathers' anxiety levels remained stable. Depression and general emotional distress at the two month follow-up were predictive of marital adjustment at the 20-month follow-up. Dahlquist et al. (1996) argued for interventions that include both parents and the marital partnership to provide

more fully integrated services to families facing cancer. Limitations include a small sample size comprised primarily of Caucasian (88%), middle income couples. Therefore, the authors stated that these findings may not generalize to minorities or low-income couples. It is also possible that more conflicted couples chose not to participate in the study, thus introducing selection bias into the sample.

Parental coping with a child's illness may influence the child's psychological adjustment (Sawyer, Streiner, Antoniou, Toogood, & Rice, 1998). Using a prospective design, researchers examined 38 families of children aged two to five who were newly diagnosed with cancer. Child adjustment and parental psychological adjustment were measured at the time of diagnosis and then two years post-diagnosis. Path analysis revealed that maternal adjustment at the time of the child's diagnosis was significantly correlated with the child's psychological adjustment two years later. This relationship was not found with paternal or family adjustment. The study is limited by its reliance on a single measure to assess child adjustment (Child Behavior Checklist), parent adjustment (General Health Questionnaire), and family adjustment (General Functioning Scale of the Family Assessment Device). Clinically, however, this prospective study reveals an important finding, namely that mothers who demonstrate psychological difficulties (i.e., anxiety, somatization, depression) when learning of their child's cancer diagnosis are more likely to have children with later psychological difficulties. A clear point of intervention is indicated, in that mothers who are determined by staff to be clinically distressed at diagnosis can be referred for treatment (Sawyer et al., 1998).

A prospective study on predictors of psychological distress in parents of pediatric cancer patients found that different characteristics and coping styles were associated with

adjustment in mothers and fathers (Hoekstra-Weebers et al., 1999). The study recruited parents (66 mothers and 62 fathers) of children with various forms of cancer, including leukemia, brain tumors, and neuroblastomas. Parents were asked to complete questionnaires assessing psychological distress, recent life events, personality characteristics, coping style, and social support at the time of their child's diagnosis and then 12 months later.

Using multiple regression analyses, results indicated that for both mothers and fathers, trait anxiety determined at the time of the child's diagnosis was a significant predictor of psychological distress at the 12 month follow-up. Pleasant life events occurring prior to diagnosis and less assertive behavior in mothers were associated with difficulties in adjustment 12 months later. The authors conjectured that even pleasant life events are stressful and require adjustment, particularly while mothers are also dealing with the trauma of childhood cancer. Quality of social support was an important predictor of adjustment in fathers. Fathers who were not satisfied with their social support networks were at increased risk for psychological distress. In contrast to mothers, unpleasant events prior to diagnosis were predictive of maladjustment in fathers (Hoekstra-Weebers et al., 1999). Few studies have explored the adjustment of fathers in pediatric populations; therefore, this study is helpful in delineating some of the differences between mothers and fathers in coping with their child's cancer diagnosis and treatment (Hoekstra-Weebers et al., 1999). The primary limitation of this study was that the small sample size did not allow for statistical analyses, such as path analysis, that might have revealed more complex relationships among the variables.

In a study of mothers of pediatric bone marrow transplant recipients, researchers examined changes in parental stress over the course of transplant and piloted an intervention program designed to help parents manage the stress of hospitalization (Streisand, Rodrigue, Houck, Graham-Pole, & Berlant, 2000). Researchers studied 22 mothers over six time points ranging from preadmission to three weeks post-transplant. Eleven mothers were randomly assigned to the intervention, whereas eleven mothers served as the control group. The intervention protocol was based on a stress inoculation model, which emphasized education, relaxation, and communication. All participants received questionnaires designed to measure types, frequency, and symptoms of stress (Streisand et al., 2000).

Results indicated that the most stressful time period for mothers was just prior to their child's admission for bone marrow transplantation. The intervention group used significantly more stress reduction techniques than the control mothers. The authors argued that the pre-admission period may be a critical time for interventions aimed at coping and stress reduction for mothers of bone marrow transplant patients (Streisand et al., 2000). One strength of this study is the prospective design and the pilot of a psychological intervention. However, the sample size was quite small, primarily due to the relative infrequency of bone marrow transplantation performed in a single hospital setting (Streisand et al., 2000).

Sloper (2000) conducted a prospective study on 68 mothers and 58 fathers of pediatric cancer patients to investigate emotional distress over time, as well as social support and coping resources. The researcher was interested in how parental distress changed over the course of illness, as well as how various life stressors, such as financial

difficulties, affected adjustment. Parents recruited from five hospitals were interviewed and completed questionnaires measuring psychological distress, demographics, recent life events, financial and employment problems, psychosocial resources, social support, locus of control, coping strategies, and appraisal of illness both six and 18 months after learning of their child's cancer diagnosis (Sloper, 2000).

Results indicated that parents experienced significant emotional distress at both time points (six and 18 months post-diagnosis). Specifically, 40% of fathers and 50% of mothers reported persistent difficulties with adjustment. In fact, there was no difference in distress between parents whose children had completed treatment and parents whose children were in the active phase of treatment. Sloper (2000) offered a possible explanation for this by citing interviews in which parents expressed significant fears of cancer recurrence and the many challenges they continued to face once the acute crisis resolved. Both mothers and fathers reported declining social support from friends and the community after their child's treatment ended. Family cohesion was important to both mothers and fathers. In addition, parents who expressed confidence in their ability to manage their child's illness expressed less distress over time (Sloper, 2000). Sloper et al. (2000) pointed to the low incidence of pediatric cancer and the difficulties in obtaining a sufficient sample. Furthermore, the study did not utilize a control group. It might also have been helpful to have data from other sources, such as the hospital staff.

Another study looked more specifically at social support and how it influences parental coping at diagnosis, as well as six and 12 months after diagnosis (Hoekstra-Weebers, Jaspers, Kamps, and Klip, 2001). Parents (N= 128) of pediatric cancer patients completed measures of psychological distress, social support, and dissatisfaction with



social support. Results indicated that parents experienced the highest levels of emotional distress and social support at the time of diagnosis, with both distress and support declining over time. When compared to a normative sample at one year post-diagnosis, however, parents of ill children continued to experience higher levels of psychological difficulties (Hoekstra-Weebers et al., 2001).

Interestingly, fathers appeared to be more affected by social support than were mothers, in that fathers reported more negative experiences with their support network. This dissatisfaction was related to higher levels of emotional distress. The authors contended that social support is a complex entity, but one that is amenable to intervention. They argued that more information is needed to understand the various ways fathers and mothers experience and desire social support at different time points in the child's illness (Hoekstra-Weebers et al., 2001). A limitation was that only self-report data was collected.

#### *Psychological adjustment of parents with children with spina bifida*

Parental coping and adjustment have also been studied in parents of children with spina bifida. In an effort to understand parental functioning and pediatric chronic illness from a family systems/social-ecological perspective, Holmbeck et al. (1997) gathered information on multiple levels of parental adjustment, including coping, adaptability to change, psychological symptomatology, parenting satisfaction, parenting stress, perceived parenting competence, and marital adjustment. Parents of eight and nine year-old children with spina bifida (55 families) were compared with a matched control group (55 families) of healthy children.

Compared with parents of healthy children, parents of children with spina bifida experienced higher levels of distress and maladjustment (Holmbeck et al., 1997). For instance, both mothers and fathers expressed less satisfaction with the parenting role. Mothers also perceived themselves to be less competent as parents, indicated higher levels of social isolation, tended to use denial as a method of coping, and scored lower on the “adaptability to change” measure than did mothers in the control group. When compared with fathers in the control group, fathers of children with spina bifida reported more frequent symptoms of emotional distress and higher levels of role restriction. The authors highlighted the need for appropriate interventions that address coping strategies, parenting, and social connection when working with parents of chronically ill children (Holmbeck et al., 1997).

*Psychological adjustment of parents of children with cardiac disease*

Parental adaptation and psychological adjustment have also been studied in the pediatric cardiac disease population. Davis, Brown, Bakeman, and Campbell (1998) examined maternal cognitive processes, including appraisal of stress, daily hassles, illness tasks, expectations, health locus of control, family functioning, maternal psychological functioning, and coping behaviors in a sample of 52 mothers of children with congenital heart disease. Results indicated that approximately 37% of mothers experienced psychological distress. Adaptive coping (which refers to coping behaviors aimed at problem-solving, seeking information and social support) and cognitive restructuring techniques were predictive of maternal adjustment; in contrast, palliative coping (which involves avoidance and self-blame) and daily stress and hassles were negatively associated with maternal adjustment. Interestingly, the severity of the child’s

cardiac illness was not related to mothers' distress (Davis et al., 1998). One limitation is that there are not established, reliable methods of assessing disease severity of congenital heart defects. Furthermore, the sample size was limited due to the low incidence of children with congenital cardiac disease.

In an attempt to uncover the primary concerns and worries mothers face when caring for a child with congenital heart disease, Van Horn, DeMaso, Gonzalez-Heydrich, and Erickson (2001) administered semi-structured interviews and questionnaires to a group of 38 mothers during their child's hospitalization and two to four weeks post-discharge. In addition, both cardiologists and mothers rated the severity of the child's cardiac illness.

Mothers of children with congenital heart disease expressed five main concerns, which were reliably grouped into the following: medical prognosis, psychosocial functioning, quality of life, effects on family, and financial issues. Primary concerns during hospitalization were the child's medical prognosis, the child's psychosocial adjustment, and the impact of the hospitalization on the family. Primary concerns when the child returned home included child's quality of life and financial issues. Furthermore, at two to four weeks post-hospitalization, there was an association between mothers' ratings of medical severity and concerns about the child's quality of life and family adjustment (Van Horn et al., 2001).

The authors contended that knowledge of these common concerns may be beneficial to the medical and psychosocial staff treating families affected by congenital heart disease. Through awareness, staff can anticipate some of these concerns and offer support and suggestions for coping. There are several limitations to consider when

interpreting the results of the study. The sample was small and consisted primarily of upper-middle class, Caucasian women who were married. Generalizability is thus limited to this group. Furthermore, the study did not include fathers in the sample. Van Horn et al. (2001) also pointed out that the children in the study tended to have more severe forms of congenital heart disease. There were 16 mothers who declined participation due to “time constraints and stress.” Therefore, the final sample may not be reflective of all of the illness related concerns of mothers of children with congenital heart disease (Van Horn et al., 2001).

#### *PTSD Symptoms among Parents of Medically Ill Children*

The diagnosis of posttraumatic stress disorder is usually associated with war veterans or victims of a crime or natural disaster. The event of potentially losing one’s child to illness is also included in the clinical criteria for PTSD, yet the research in this area is minimal. The studies that do exist have focused on examining PTSD and posttraumatic stress symptoms in parents of pediatric oncology patients, transplant recipients, and, more recently, parents of newly diagnosed diabetes patients. A review of this literature will be provided to outline the specific needs and limitations of the current research and to demonstrate the need for further investigation into the experience of PTSD in parents of medically ill children.

In a recent review article, Alonzo (2000) argued that the concept of posttraumatic stress has been significantly overlooked in research on chronic illness. He postulated a general framework by which to view the traumatogenic potential that can ensue as a result of a chronic illness or of witnessing the effects of chronic illness on another person. Chronic illness, such as cardiac disease, is conceptualized as an accumulative stress that

often occurs in the context of other, more common life stressors (ie., divorce, financial burden). PTSD is viewed along a continuum, with some individuals responding with common symptoms of anxiety whereas others progress to clinical levels of posttraumatic stress. The notion of “subclinical PTSD” is also considered, in that individuals may not meet every criteria for a PTSD diagnosis, but their sub-threshold symptoms may still generate considerable disruption in their lives. Alonzo (2000) theorized that as individuals move toward clinical PTSD, their ability to cope effectively with the multiple demands of a chronic illness, such as frequent appointments, hospitalizations, and complicated medication regimens, becomes significantly compromised. In parents, this may be translated into increased difficulties meeting the medical, psychosocial, and emotional needs of their chronically ill child.

Although PTSD has traditionally been understood as resulting from a single trauma, Alonzo (2000) suggested that chronic trauma may have an additive effect, particularly when it occurs in conjunction with pre-morbid psychopathology or maladaptive coping patterns. Different layers of trauma exist when a chronic illness, such as cardiomyopathy, is discovered. Primary traumas include learning of the illness; experiencing the fear of possible death and disability; and the realization that one’s work, social, and family life will likely dramatically change as a result of the illness and treatment. Secondary traumas involve the ensuing experiences that result from the illness, such as hospitalizations, trips to the emergency room, frequent doctor’s appointments, and repetitive invasive procedures. Finally, tertiary traumas may involve one’s interactions with managed care, billing for medical services, and worries over insurance coverage. Alonzo (2000) emphasized that this multiplicity of stressors may

dramatically reduce an individual's ability to manage medical treatment, possibly resulting in non-adherence to medical recommendations.

It is also important to keep in mind that although medical treatments are designed to help ease the patient's symptoms and increase their longevity, treatment is often invasive, time-consuming, and painful. Additionally, medications, although necessary for survival, often have negative side effects (Alonzo, 2000). For instance, the steroids that pediatric heart transplant patients take to help fend off the body's rejection of the new heart can have side effects of weight gain, acne, moon facies, and truncal obesity. While steroids may keep the patient alive, they may also contribute to poor self-image, teasing from peers, and school avoidance.

Alonzo (2000) stipulated that multiple medical procedures and treatments from various services (i.e., radiology, physical therapy, dialysis, infectious diseases), although in and of themselves do not constitute devastating events, are nevertheless noxious and wear the patient and family down over time. Additionally, health care personnel may become desensitized to different medical procedures such as cardiac catheterizations; however, they are small traumas that the patient and parents must endure repeatedly. Again, the cumulative nature of these procedures may constitute a traumatogenic response from patients and parents.

Recently, investigators have begun to approach the process and experience of life threatening illness as a traumatic event. Based on clinical observation and noted gaps in the literature regarding the long-term psychosocial adjustment of chronically ill patients and their families, researchers began to postulate that posttraumatic stress might serve as an appropriate model through which to understand this population.

For example, Stuber, Christakis, Houskamp, and Kazak (1996) applied a posttraumatic stress model to a successfully treated sample of pediatric cancer patients and their families. Participants were recruited from two medical centers on the east and west coasts. Research criteria stipulated that patients had to be in remission from cancer for at least two years. Mothers (n = 63), fathers (n = 42), and cancer survivors (n = 64) completed the Posttraumatic Stress Disorder Reaction Index. Results yielded interesting findings, in that parents reported higher levels of posttraumatic stress than did survivors (40% of mothers, 33% of fathers, and 12% of survivors). In some cases, these symptoms were reported up to 12 years post-treatment. Given that only one measure was used, the data should be interpreted cautiously. In addition, given the low rates of participation (less than 60% at each site), the data may not be fully representative of parents of pediatric oncology patients. The authors speculated that the most stressed families may have found participation too overwhelming or upsetting. They argued that these findings substantiate a need for further research to examine the link between medical illness and symptoms of trauma, particularly in parents (Stuber et al., 1996).

Similar findings were observed in a larger study (N = 309) comparing posttraumatic stress symptoms in pediatric cancer survivors and their parents with a group of healthy controls (Barakat et al., 1997). Survivors were required to have completed treatment for at least one year. The comparison group, recruited from pediatric practices, did not evidence chronic illness. When completing measures of posttraumatic stress, the cancer survivors and their families were instructed to refer to the cancer experience, whereas the comparison group was told to respond based on a significant life stressor. Barakat et al. (1997) found that parents of pediatric cancer

survivors demonstrated a host of posttraumatic stress symptoms (PTSS), including intrusive memories, hypervigilance, and avoidance of reminders of cancer. Levels of PTSS in parents of survivors were significantly higher than those in comparison parents. Interestingly, parents of survivors again expressed more intense and frequent symptoms of posttraumatic stress than did their children who had survived cancer (Barakat et al., 1997). Again, this study highlights the importance of research directed at investigating how parents respond to the experience of having a child with a life threatening illness. There were several limitations to the study. First, the response rate for returning the questionnaires was 56%. A frequently cited reason for non-participation was not wishing to discuss the painful topic of childhood cancer. There may be a selection bias, and one could speculate that the most severe cases of posttraumatic stress were not examined because families self-selected out of the study. Additionally, the data were collected by mail, and thus there was no assurance that the measures were completed independently.

Posttraumatic stress symptoms in parents were also documented in a study of 130 pediatric cancer survivors (at least one year post-treatment) and their parents and 155 comparison families (Kazak et al., 1997). The authors noted that although past studies had confirmed the presence of psychological difficulties in a subset of pediatric cancer patients and their families, the specific nature of posttraumatic stress symptoms had not been adequately investigated. They hypothesized that the survivors and their parents would exhibit higher levels of anxiety and posttraumatic stress symptoms. Participants completed measures designed to assess posttraumatic stress symptoms, anxiety, family functioning, and social support.



Kazak et al. (1997) found that parents of cancer survivors showed significantly more trauma symptoms than comparison parents. Families suffering from posttraumatic stress were also more likely to endorse communication difficulties and decreased family satisfaction. Interestingly, pediatric cancer survivors did not differ significantly from their comparison peers on posttraumatic stress symptoms. The authors postulated that many of the children were very young at the time of treatment (median age of onset for leukemia is three to four years of age). Therefore, these children may not have remembered the nature or course of their treatment, or they may not have had the cognitive/developmental capacity at the time to fully comprehend the seriousness of their condition. Kazak et al. asserted that children may process illness-related trauma differently from adults. This study is important in documenting the presence of posttraumatic stress in parents of cancer survivors. The authors caution that the measures used to assess posttraumatic stress symptoms in children were originally designed to measure symptoms in response to an acute event (i.e., violence), rather than an ongoing trauma (i.e., chronic childhood illness). This measurement limitation should be taken into account. Measures that are geared toward assessing PTSD related to an illness is an important area in need of future research (Kazak et al., 1997). These studies highlight an emerging finding that parents may be more stressed and/or traumatized than their children in the aftermath of a life-threatening illness.

Another investigation attempted to predict posttraumatic stress symptoms in parents of pediatric cancer survivors by examining trait anxiety, perceptions of cancer threat, family functioning, social support, treatment experiences, and events occurring post-treatment (Kazak et al., 1998). Researchers categorized the above-mentioned

variables as falling within one of four areas: personality variables, current individual and family systems variables, treatment events, and post-treatment variables. These predictor variables were examined as they related to the outcome variable, which was posttraumatic stress experienced by parents. A total of 331 families (320 mothers, 224 fathers, and 320 survivors) participated in the study. Questionnaire packets were sent out to each individual, with a return rate of 56%. Researchers found that trait anxiety in both mothers and fathers was significantly related to posttraumatic stress symptoms. Additionally, parents who continued to worry about their child's mortality despite successful treatment were more likely to demonstrate posttraumatic stress symptoms. There were many parents who chose not to participate in the study, citing "not wanting to revisit a painful event." Indeed, the authors conjectured that avoidance is a major symptom of posttraumatic stress, and it is possible that some of these families declined participation as a result of posttraumatic symptomatology (Kazak et al., 1998).

In addition to studying posttraumatic stress, Manne, DuHamel, Gallelli, Sorgen, and Redd (1998) also examined the co-morbidity of depressive and anxiety disorders in mothers of pediatric cancer survivors. Through clinical interview and self-report measures administered to 65 mothers, Manne et al. (1998) found that 6% currently experienced a clinical diagnosis of PTSD, and an additional 20% had subclinical PTSD (2 out of 3 criteria). Finally, comorbidity of clinical depression or anxiety occurred for 25% of mothers with a diagnosis of PTSD (Manne et al., 1998).

A study examining posttraumatic stress disorder in adult heart transplant patients and their primary caregivers postulated that heart transplantation, although often a life saving procedure, can be traumatic due to the wait for a donor heart, the resulting guilt

from knowing that a heart can only be received if someone else dies, and the lifelong post-transplant follow-up and care (Stukas et al., 1999). Adult heart transplant recipients (n= 158) and their primary caregivers (n= 142) who were part of a larger prospective study examining post-transplant health, were interviewed two months, seven months, and 12 months after surgery. They were asked about posttraumatic stress symptoms, psychiatric history, family psychiatric history, social support, and coping strategies. Results indicated that 10% of heart transplant patients and 8% of primary caregivers met full criteria for PTSD. Further studies with this population found that, after controlling for other predictors of mortality, heart transplant patients with PTSD during the first year post-transplant had a 13 times greater mortality rate three years post-transplant than those without PTSD. Additionally, family caregivers were demonstrated to be at-risk for post-traumatic stress symptoms, and Stukas et al. (1999) argued that the proximity to the ongoing trauma puts caregivers at increased risk.

The impact of posttraumatic stress symptoms on parental functioning may not be limited to the time of the child's illness. Barakat, Kazak, Gallagher, Meeske, and Stuber (2000) found that parental posttraumatic stress symptoms did indeed have long-term consequences, even after the child had achieved remission. They prospectively examined posttraumatic stress symptoms in childhood cancer patients and their mothers and how these symptoms were associated with later psychological adjustment. Additionally, other life stresses and appraisals of threat and intensity of cancer treatment were taken into account. The study was comprised of two time points (Time I and Time II), and involved patients and mothers from medical centers on both the east and west coasts. At the initiation of the study (Time 1), 332 families participated in the study by mailing back

questionnaire packets that assessed posttraumatic stress and appraisal of cancer threat. At Time II, approximately 18 months later, only families who lived within a two-hour drive of the hospital were contacted. During this phase of the study, participants were interviewed and completed measures that assessed stressful life events/life experiences, child adjustment, and parental psychopathology. For the purposes of this project, a total of 65 families participated; therefore, 56 childhood cancer survivors and 65 mothers of survivors comprised the sample.

Barakat et al. (2000) found that posttraumatic stress symptoms during treatment in both survivors and mothers were significantly positively related to adjustment difficulties 18 months later. In addition, stressful life events contributed to adjustment difficulties above and beyond the influence of posttraumatic stress symptoms. The authors argued that posttraumatic stress symptoms affect child and parent adjustment over time. They suggested that distress resulting from the illness may present a significant challenge as families try to continue with the demands and occurrences of daily life. Finally, the researchers advocated for the development of relevant prevention and intervention programs that target these symptoms at the time of the cancer treatment.

A prospective study of parents of pediatric leukemia patients investigated the relationship between parental anxiety during initial treatment and posttraumatic stress symptoms at follow-up (Best, Streisand, Catania, & Kazak, 2001). Participants were 67 families (66 mothers and 47 fathers) of children with a history of pediatric leukemia (91% acute lymphocytic leukemia, 9% acute myelogenous leukemia). During the initial phase of treatment (between 1991 and 1995), participants were part of a randomized clinical intervention trial investigating distress during treatment procedures. Parents

completed measures of anxiety and parenting distress. During the follow-up portion of the study (1998-1999), parents whose children were in remission from cancer completed measures assessing current level of state and trait anxiety, social support, posttraumatic stress symptoms, parental avoidance, and self-efficacy.

Best et al. (2001) found that mothers who were highly anxious during their child's cancer treatment were more likely to demonstrate PTSS years later. Clinically, this was quite significant, given that PTSS includes anxiety, intrusive thoughts, and avoidance of feared stimuli. The authors noted that some parents reported avoidance of follow-up doctor's appointments, which is particularly critical with pediatric cancer patients. They pointed out that the medical consequences of avoidance and/or non-adherence are quite serious. One limitation of this study was that there were 24 families who refused to participate at follow-up, thus eliciting concerns about the sample. Interestingly, the authors suggested that the most traumatized families may have been too stressed or anxious to participate in a study that reminded them of a very painful and frightening time in their lives.

Posttraumatic stress and PTSD have also been linked to physiological dysregulation. Glover and Poland (2002) examined cortisol, norepinephrine, and epinephrine levels in 14 mothers with PTSS and seven mothers without PTSS. All mothers (total of 21) had children who were cancer survivors. Diagnoses of posttraumatic stress disorder were determined through the use of the Posttraumatic Stress Diagnostic Scale (PDS) in a telephone interview. In addition, there were eight mothers of healthy children who served as the control group. All mothers provided an overnight urine sample. The data yielded interesting findings, in that mothers of cancer survivors

with PTSD had significantly lower urinary cortisol levels and higher urinary norepinephrine than did mothers without PTSD and control mothers. The authors pointed out that reduced cortisol and increased norepinephrine levels have been documented in individuals with PTSD through exposure to war and sexual abuse. These results should be interpreted with caution, however, given the small sample size and the non-representative nature of the sample (i.e., predominantly Caucasian).

A recent multi-site study found evidence that social support and cognitive processes were important in predicting maternal posttraumatic stress after pediatric bone marrow transplantation (Manne et al., 2002). Manne et al. studied 90 mothers of children undergoing bone marrow or hematopoietic stem-cell transplantation at the time of transplant, three months post-transplant, and six months post-transplant. Mothers completed questionnaires at three different time points assessing posttraumatic stress symptoms, exposure to trauma, anxiety, depression, and social support. A subset of mothers participated in a clinical interview at the third time point to assess for PTSD. Results indicated that cognitive processes, including appraisal of threat and fears for the child's later functioning, were predictors of traumatic symptoms in mothers at the six-month follow-up. Furthermore, anxiety and depressive symptoms at the time of transplant were predictive of later posttraumatic stress symptoms, as was negative feedback from family and friends. In other words, those mothers with signs of psychopathology or negative cognitive processes at the time of the child's diagnosis were more susceptible to posttraumatic stress symptoms through the illness and recovery process. Therefore, the authors concluded that it is important to address symptoms of fear, anxiety, and depression in parents during the early part of the transplant process.

Limitations of the study include the fact that posttraumatic stress symptoms may have been present prior to the child's transplant. Additionally, some mothers did not participate in the six month follow-up, and it is possible that those mothers were more traumatized and thus more likely to avoid reminders of the event (Manne et al., 2002).

A recent pilot study investigated the occurrence of PTSD and PTSS in a sample of parents of children with newly diagnosed type I diabetes (Landolt et al., 2002). Given that prior research had indicated trauma symptoms in parents of other medically ill children (ie., pediatric cancer), Landolt et al. were interested in determining if a trauma model could be applied to parents of diabetic patients. Study participants consisted of mothers and fathers of 38 children (14 girls and 24 boys) who were newly diagnosed with Type I diabetes. One measure was administered, the Posttraumatic Diagnostic Scale, a self-report questionnaire that provides a diagnosis of PTSD based on DSM-IV criteria and provides an indication of the severity of PTSD symptoms. Researchers defined "subclinical PTSD" as individuals who endorsed at least one symptom in each area of PTSD: re-experiencing of the trauma, avoidance, and arousal. Mothers and fathers were mailed the questionnaire packets approximately six weeks after their child was diagnosed with diabetes.

Results indicated that 24% of mothers and 22% of fathers met the full diagnostic criteria for PTSD, with an additional 51% of mothers and 42% of fathers meeting the criteria for sub-clinical PTSD. The authors reported that these rates of PTSS were significantly higher than rates found in community samples, suggesting that the posttraumatic symptoms were associated with the onset of type I diabetes in their child.

Landolt et al. cautioned, however, that results were based upon a relatively small sample (N = 38), a control group was not used, and there was only one measure of PTSD.

Most recently, researchers examined the incidence of PTSS in parents of pediatric solid organ transplant recipients, including liver, kidney, and/or heart transplant (Young et al., 2003). Young et al. hypothesized that parents of pediatric transplant patients would endorse significant levels of posttraumatic stress in the years following their child's transplant surgery. Participants were primary caregivers of heart transplant patients (n = 31), liver transplant patients (n = 92), or kidney transplant patients (n = 46) who completed measures of posttraumatic stress, depression, anxiety, family stress, and social support. Parents completed the measures either in person or over the telephone.

Results revealed that 51% of parents endorsed PTSS in the moderately severe range. Approximately 27% of parents met diagnostic criteria for a clinical diagnosis of PTSD based on the DSM-IV (Young et al., 2003). Stepwise regression analyses revealed that parent's perceptions of their child's physical health significantly predicted PTSS. Therefore, regardless of the child's medical prognosis, parents who perceived the greatest threat to their child's physical health were more likely to evidence PTSS. Additionally, parents who endorsed high family burden (i.e., the feeling that the transplant negatively influenced family life) demonstrated higher PTSS. This study supports the notion of viewing the transplant experience as a potentially ongoing trauma and highlights parents of pediatric transplant patients as an at-risk population (Young et al., 2003). One limitation of the study is that it only used self-report measures; the authors contended that future studies should utilize multiple assessment methods. Furthermore, stepwise



regression analyses were used, which capitalize on chance; it may have been more sound to use hypotheses to guide the analyses.

### *Summary*

What becomes apparent in this review of the literature is the growing recognition that parents of medically ill children often develop PTSS. As noted in the above review, the majority of research on posttraumatic stress has focused on parents of pediatric cancer patients. The literature indicates that parents are indeed traumatized by a child's illness, and many met full criteria or were considered to meet sub-threshold levels of PTSD.

Some authors have postulated that in parents of medically ill children, symptoms of avoidance ("efforts to avoid activities, places, or people that arouse recollections of the trauma," APA, 1994, p. 428), may translate into non-adherence with medical recommendations. For instance, parents may prolong making follow-up appointments or become increasingly symptomatic (i.e., agitated, anxious) when required to return to the hospital for treatment. Over time, these behaviors may develop into a pattern of non-adherence to the medical regimen, with potentially devastating consequences to the child's health. Thus, an overview of the literature on medical adherence is provided to document the current need for research on those factors that are associated with poor adherence.

### *Medical Adherence*

Adherence in the medical literature is generally defined as patient behaviors that are in alignment with medical advice (Thompson & Gustafson, 1996, Haynes, 1979). For instance, adherence may be conceptualized as keeping medical appointments, taking medications appropriately, and/or following recommended dietary guidelines (Lemanek,

2003). The behaviors patients are asked to adhere to depend upon their illness and current level of health. In medical settings, adherence is generally viewed as an important component of treatment, in that it helps to facilitate treatment goals and, hopefully, leads to improved health of the patient (Thompson & Gustafson, 1996). Given that estimated rates of non-adherence in chronically ill populations range from between 50% and 55%, the issue of adherence represents a serious problem to patients and health care providers attempting to produce positive health outcomes (Dunbar-Jacob et al., 2000).

The terms “adherence” and “compliance” are frequently used interchangeably to indicate the same construct in the medical literature, although the move toward “adherence” reflects the changing attitudes toward patient involvement and empowerment. Medical compliance is an older term that connotes obeying authority figures (the physician), while the term adherence implies choice and a partnership between the patient and physician (Leventhal, 1993).

Both clinically and in research studies, operationalizing the concept of adherence can be challenging. One method of operationally defining adherence involves setting cut-off scores in which patients are categorized as either “adherent” or “non-adherent” to the medical regimen. Another method involves collecting different indices of adherence and creating one overall score. (La Greca & Schuman, 1995). There is not much literature and knowledge about adherence, particularly in chronic illness populations, in part because the construct itself is difficult to measure. In fact, there is not a “gold standard” for measuring adherence (Lemanek, 2003).

Measurement of adherence can be broken down into direct and indirect methods (Epstein & Cluss, 1982). Direct measurement methods involve examining blood levels and/or urinalysis testing to detect the presence of the prescribed medication in the body. Indirect measurement methods rely upon self-report questionnaires, physician ratings, and/or pill counting (Epstein & Cluss, 1982).

There are multiple consequences of non-adherence that make it an important focus of concern for health care providers and medical researchers. Perhaps the most adverse consequence of non-adherence is increased mortality (Lemanek, 2003). Particular medical conditions, such as AIDS and organ transplantation, require very high adherence rates to maximize the benefits of the treatment regimen and avoid disease. Lapses in adherence could lead to increased symptoms, frequent hospitalizations, and/or organ rejection.

In the case of heart transplant recipients, rejection can be a matter of life or death. In contrast, dialysis remains an option for kidney disease if the new kidney is not functioning well. In the heart transplant population, however, there are very few options available when faced with chronic rejection of the new heart. Therefore, adherence becomes an extremely important factor in maintaining the health of the patient. In fact, when patients and families are being evaluated for placement on the heart transplant list, the family's likelihood to adhere to the medical regimen is one of the criteria medical staff uses to determine eligibility. The medical team looks very seriously into whether or not the family demonstrates the ability, organization, commitment, and resources to follow through with the intensive post-transplant protocol. If a family has a history of non-adherence, and there are significant questions regarding their ability to manage the

regimen, there is the possibility that the child will not be placed on the heart transplant list because of the shortage of hearts available for transplant (Cimato & Jessup, 2002).

Research indicates that transplant patients who report missing medications were over four times more likely to experience rejection (Dew et al., 1999). Ringewald et al. (2001) found that non-adherence with prescribed medical regimens was associated with organ rejection and poor medical outcome (morbidity and mortality) in pediatric heart transplant recipients. Researchers and clinicians alike are interested in learning about those factors associated with adherence, so that appropriate interventions can be designed to help patients and families maximize their chances of success following transplant.

Researchers have found that chronic disease, as opposed to acute disease, is typically associated with increased risk of non-adherence (Dunbar-Jacob et al., 2000). Individuals with a solid organ transplant have essentially traded an acute illness (i.e., renal failure, congestive heart failure) for a chronic post-transplant course with long-term side effects. The chronic nature of the transplant population puts them at risk for non-adherence. Additionally, Dunbar-Jacob et al. (2000) pointed out that complex medical regimens, involving frequent medications and hospital procedures, typically reduce adherence. Medication side effects also commonly result in decreased adherence. For instance, steroid treatment is necessary post-transplant to help ensure that the body does not reject the transplanted organ. However, children often develop unwanted side effects (i.e., weight gain, acne, and increased hair growth), which are associated with poor adherence (LaGreca & Schuman, 1995).

Adherence research in pediatric populations began primarily with investigations of diabetes, asthma, and juvenile rheumatoid arthritis populations. Although a review of

the literature on adherence in these populations is beyond the scope of this literature review, studies of these conditions in children have resulted in some consistent findings. First, children with emotional or behavioral difficulties were less likely to be adherent with their prescribed medical regimens (Brownbridge & Fielding, 1994). Furthermore, patients with less knowledge and understanding about their illness were more likely to be non-adherent (La Greca, Follansbee, & Skyler, 1990). Finally, poor parental coping in these populations was associated with decreased adherence in children (Wynn & Eckel, 1986). However, less is known about adherence issues in organ transplant populations, which is the focus of the proposed study. To further elucidate the factors associated with non-adherence in the proposed study population, the literature on adherence in pediatric organ transplantation and adult heart transplantation will be reviewed.

#### *Adherence in Pediatric Renal Disease/Renal Transplantation*

In an effort to better understand the factors contributing to non-adherence, Meyers, Thomson, and Weiland (1996) studied the knowledge and attitudes of 56 pediatric renal transplant patients and their parents toward medical adherence. The children ranged in age from 2 to 21 years, and each completed one questionnaire that was developed by the research team and administered by a nurse in the nephrology department. Parents of children under 10 years of age completed the questionnaire in conjunction with their child, whereas children over 10 years completed the questionnaire by themselves. The questionnaire inquired about the patient and parents' understanding of the disease and medical regimen, perceptions of their own adherence, and their feelings about the communication and education given by the medical team. Non-adherence was determined if the patient or parent reported not taking immunosuppressive

medication or not taking it as prescribed. Additionally, patients were coded as non-adherent if their medication had run out due to missed clinic visits (Meyers et al., 1996).

Based upon the aforementioned criteria, the non-adherent and adherent groups were compared along several dimensions. The groups differed in their understanding of renal disease, renal transplant, and immunosuppressive therapy, with the non-adherent group demonstrating less knowledge. Patients in the non-adherent group were less likely to remember the names of their medications and took them less often. Over half of patients and their parents desired more information about renal transplantation and medication therapies (Meyers et al., 1996).

Several limitations of this study exist. First, only one questionnaire was used, and it is not clear if and how reliability and validity were established. The study relied solely on a self-report measure, which can lead to biased results (i.e., patients might be hesitant to report not taking their medications to a nurse in the nephrology department). Additionally, some of the children completed the measure individually, while some completed it with their parents. This might also have resulted in biased reporting, in that children might have responded differently if completing the measure alone. Furthermore, the methodology did not clearly specify the cut-off points for the adherent and non-adherent groups. In general, there is no clear standard or specified set of criteria for “diagnosing” adherence (Meyers et al., 1996).

In a study of adolescent renal transplant patients, Blowey et al. (1997) were interested in documenting and describing patterns of non-adherence with the immunosuppressant medication, cyclosporine. The authors asserted the importance of examining adherence in transplant populations, given that “the greatest weakness in the

therapeutic chain remains the patient's behavior" (p. 547). Research subjects were recruited based upon the following criteria: renal transplant recipients between 12 and 18 years of age who were at least one year post-transplant and currently taking cyclosporine capsules. A total of 19 adolescent transplant patients participated in the study.

To assess adherence, electronic monitors (MEMS caps, which stand for "Medication Event Monitoring Systems") were used. The monitors were part of the patient's medication bottle cap and recorded the time and date the medication bottle was opened. When using electronic monitors to assess adherence, it is assumed that each instance the bottle is opened represents a dosage taken by the patient. Adherence was defined categorically in this study, such that patients were considered non-adherent if their percentage of cyclosporine doses was below 80% (Blowey et al. 1997).

Members of the transplant team, comprised of pediatric nephrologists and nurses, rated the likelihood of adherence for each patient on a linear scale based on their past experience of the patient. Patients were also interviewed on their adherence behaviors, and queried about how often they took their medications, why they might not have taken their medications, and whether or not the electronic monitor had any effect on their behavior. Additionally, blood levels of cyclosporine were collected. Patients were considered non-adherent if the cyclosporine concentration in their blood was below 50 ng/ml (Blowey et al., 1997).

A mean of 165 doses of cyclosporine were recorded from the MEMS device for each patient. Adherence rates ranged from 64% to 100%, with a mean of 91%. Four patients (21%) were categorized as non-adherent based upon the above-mentioned criteria, whereas five patients evidenced more than three consecutive missed doses.

Furthermore, there was a “downward trend” in medication adherence over the three-month study period (Blowey et al., 1997).

This study is helpful in documenting adherence difficulties in adolescent transplant populations. However, there are several methodological limitations to consider. First, the sample size of 19 patients was quite small. Unfortunately, this is a common limitation in research studies with transplant populations, given the relative infrequent occurrence of organ transplants, which results in a finite population within which to gather study data. Despite the small sample size, however, interesting data can still be gleaned from the study. A second limitation lies in the potential misuse of the electronic pill counting device. The MEMS device does not measure whether or not the patient actually ingested prescribed medications, only if the bottle was opened during the observation period. It was presumed that an opened bottle meant that the patient took the medication. MEMS devices are quite expensive and thus not frequently used in adherence studies. However, electronic monitoring devices represent a relatively new assessment method that may provide additional data in the rather difficult practice of measuring adherence in medical populations (Blowey et al., 1997).

A longitudinal study of adolescent renal transplant patients examined the relationship between psychological functioning and medical adherence (Penkower et al., 2003). The sample consisted of 22 renal transplant patients (ages 13-18) and their caregivers. Adolescent patients were interviewed about their adherence practices at the start of the study and then approximately 12 months later. The interview inquired about the frequency of taking transplant medications, as well as missed appointments. The study categorized adolescents as non-adherent if they failed to take prescribed



medications three or more times in one month or did not attend a lab appointment or clinic visit. Adolescents and caregivers completed questionnaires at both time points that assessed the adolescent's psychological functioning in three primary areas: depression (Beck Depression Inventory), anxiety (Spielberger State-Trait Anxiety Scale), and anger (Spielberger State-Trait Anger Scale).

Penkower et al. (2003) found that anxiety symptoms in adolescent renal transplant recipients (36%) were double those reported in community samples (9%-17%). Non-adherence rates in this population were found to be 13.6%. Furthermore, anger was the strongest predictor variable of medication non-adherence. This study was limited in its statistical power due to the small sample size, and thus the results must be interpreted cautiously (Penkower et al., 2003).

In an effort to document rates of non-adherence in pediatric renal transplant patients and delineate the factors contributing to non-adherence, Shaw, Palmer, Blasey, and Sarwal (2003) performed a retrospective chart review consisting of demographic data, type of insurance, age at transplant, number of renal biopsies, graft function, and graft loss. Physician ratings of non-adherence and determinations of primary reasons for non-adherence were collected, as well as blood levels of immunosuppressant medications. Additionally, patients were administered a psychosocial diagnostic interview by a mental health clinician.

Of the 112 pediatric renal transplant recipients examined, 32% were considered non-adherent to the medical regimen based on immunosuppressant blood levels and physician report (Shaw, Palmer, Blasey, & Sarwal, 2003). Based upon their experience, physicians identified the primary reasons for non-adherence as lack of parental

involvement in the child's treatment and parent-child conflicts. Additionally, of those patients considered non-adherent, approximately 30% had a psychiatric diagnosis. The authors noted that since approximately 7% of patients eventually lose their transplanted kidney as a result of non-adherence, it is important for research and medical staff to target and address factors that affect non-adherence.

#### *Adherence in pediatric liver transplantation*

Lurie and colleagues (2000) were interested in investigating the risk factors associated with severe medical non-adherence. Due to the lack of a sufficient sample size, this study was conceptualized as a preliminary, descriptive investigation on adherence in pediatric liver transplant patients. The design employed a retrospective chart review of a total of 18 patients. Three patients comprised the severely non-adherent group and met the following criteria: greater than one year of documented non-adherence and organ loss/death. Fifteen patients comprised an age-matched cohort of pediatric liver transplant patients who were not considered to be severely non-adherent (Lurie et al., 2000).

The two groups were compared on 27 variables investigators collected through chart review. Such variables were determined by the researchers to be potentially related to non-adherence and included socioeconomic status, family constellation factors, psychiatric diagnosis, physical or sexual abuse, school difficulties, and substance abuse. A comparative analysis revealed that the severely non-adherent group was more likely to live in single parent homes, have a family or individual history of substance abuse and/or child abuse, carry a psychiatric diagnosis, receive public assistance, and not attend school. (Lurie et al., 2000). This study has several limitations, and the authors

emphasized the preliminary nature of their findings. The sample size was extremely small, particularly in the severely non-adherent group. Therefore, statistical analyses could not be performed beyond a comparative analysis between the two groups. Thus, the study provided limited information into those factors associated with adherence. The study could, however, inform future studies regarding variables in need of future study (i.e., the potential role of physical/sexual abuse in adherence) (Lurie et al., 2000).

In an initial attempt to document posttraumatic stress in pediatric liver transplant patients, Shemesh et al. (2000) examined the relationship between PTSS and non-adherence. The researchers acknowledged the scarcity of data on those factors that contribute to non-adherence in pediatric patients, and hypothesized that those pediatric patients who demonstrated PTSS would evidence lower levels of medical adherence. Nineteen pediatric liver transplant recipients completed interviews designed to assess PTSS. Adherence was measured by assessing blood levels of tacrolimus (an immunosuppressant) and by obtaining ratings of adherence from two hepatologists and a clinical nurse. The study revealed a significant correlation between PTSS and medical non-adherence in pediatric liver transplant recipients. The authors pointed out that small sample size and the lack of a “gold standard” for measuring adherence were limitations of the study (Shemesh et al., 2000).

#### *Adherence in pediatric heart transplantation*

In the first empirical study to examine adherence in pediatric heart and heart-lung transplant patients, a sample of 53 children/adolescents and their families (29 heart transplant patients and 24 heart-lung transplant patients) were followed up at approximately 12 months post-transplantation (Serrano-Ikkos, Lask, Whitehead, &

Eisler, 1998). Children participated in a semi-structured interview designed to assess psychiatric symptoms and treatment adherence. To diagnose psychiatric disorder, the interviews were coded according to the International Classification of Mental and Behavioral Disorders Classification System. Two investigators completed the interviews, and interrater reliability was established. Information on the child's self concept, home and school behavior, and global functioning were gathered.

Additionally, parents were administered the Camberwell Family Interview Schedule, which provides ratings of family criticism, positive remarks, overinvolvement, warmth, and global family adjustment. Parents also completed measures assessing their psychosocial and marital adjustment. To assess adherence, children and parents kept a diary in which they recorded medication times and dosages. Additionally, cyclosporine levels were monitored. Children were considered adherent if their cyclosporine levels were within 80%-100% of the expected range and the medical diaries were fully completed (Serrano-Ikkos et al., 1998).

Results indicated that approximately one third of the children were non-adherent to the medical regimen based upon their cyclosporine levels and medical diaries. Family functioning variables were associated with non-adherence. Specifically, low levels of maternal warmth and high levels of maternal hostility and criticism were associated with poor adherence (Serrano-Ikkos et al., 1998). The use of medical diaries to assess adherence may be a potential limitation of the study, in that children and/or parents may complete them "correctly" due to social desirability factors and not wanting to admit failure to follow medical advice.

One study sought to identify the association between non-adherence and rejection in a sample of 50 pediatric heart transplant patients (Ringewald et al., 2001). The authors hypothesized that medication non-adherence would be significantly associated with organ rejection. The methodology included a retrospective chart review in which the number of rejection episodes, defined as a “clinical event in which immunosuppressive therapy was augmented,” was counted (p. 2). A diagnosis of rejection was made due to either difficulty noted on an echocardiogram, problematic cardiac biopsy results, and/or an autopsy. Non-adherence to the medication regimen was determined by examining the patient’s levels of cyclosporine, an immunosuppressant, at the time of rejection. Non-adherence was determined if the concentration of cyclosporine in the patient’s blood was  $< 83$  mmol/L or  $> 373.5$  mmol/L (Ringewald et al., 2001).

Results indicated that medication non-adherence was indeed correlated with episodes of rejection in this population. Furthermore, rejection episodes were associated with increased mortality (Ringewald et al., 2001). The authors reported that approximately 40% of the sample was non-adherent. These findings highlight the dire consequences of non-adherence (i.e., death) following pediatric heart transplantation. However, one limitation to consider when interpreting these findings is that the authors defined adherence through one biological marker, cyclosporine levels, rather than with multiple measures. Ringewald et al. (2001) contended that although immunosuppressive medication levels are often signs of non-adherence, levels might vary as the result of an unknown factor.

### *Adherence in Adult Cardiac Illness and Heart Transplantation*

One prospective study examined the prevalence and predictors of non-adherence in a sample of 86 heart transplant patients throughout a 12 month period (Dew, Roth, Thompson, Kormos, & Griffith, 1996). Individuals were interviewed two months, seven months, and 12 months post-transplantation on eight areas of adherence (medication, clinic attendance, completing blood work, monitoring blood pressure, exercise, diet, smoking, and substance use). The patient's primary caregiver completed a separate interview about the patient's adherence in these eight domains. The nurse practitioner also provided information about the patient's adherence to the medical regimen. At two months post-transplantation, patients completed measures assessing levels of depression, anxiety, anger-hostility, and sense of control over their lives. Coping style was examined, specifically the use of active behavioral coping, active cognitive coping, and avoidance coping. Social support was also assessed by examining the patient's relationship with their primary caregiver (generally a spouse) and perceived support from friends (Dew et al., 1996).

Prevalence rates for non-adherence in the various domains ranged from 6% (heavy drinking) to 37% (exercise). Approximately 20% of patients were non-adherent with their medication regimens. Furthermore, adherence declined over the course of the year. Hierarchical regression analyses indicated that anxiety at two months post-transplantation significantly predicted non-adherence at seven and 12 months post-transplant. Dew et al. (1996) reported that heart transplant patients with symptoms of anger and hostility were approximately 13 times more likely to demonstrate medication non-adherence. The use of avoidant coping strategies significantly predicted medication

non-adherence, as well as adherence to getting blood work done regularly, taking blood pressure, exercise, and diet. Furthermore, a poor relationship with the primary caregiver was negatively associated with adherence. Limitations include using only self-report measures of adherence, although there was high concordance among the multiple informants rating adherence (Dew et al., 1996).

In another prospective study, Dew and her colleagues (1999) examined adherence, psychological functioning, and mortality in 145 adult heart transplant patients during the first year post transplant and then three years post transplant. They were interested in whether or not adherence and psychological adjustment throughout the first year post-transplant predicted morbidity and mortality at follow-up. During the first year after a patient's heart transplant, they completed individual interviews and self-report questionnaires that assessed adherence to the medical regimen, depression and anxiety-related disorders, anger-hostility, and posttraumatic stress. The patient's primary family caretaker completed an interview of the patient's adherence behaviors as well. Morbidity and mortality were determined through the following criteria: if the patient experienced acute graft rejection, developed cardiac allograft disease, and/or death (Dew et al., 1999).

Results indicated that adherence decreased over time, including failure to regularly take medications and attend clinic appointments. During the first year post-transplant, 16% of patients were diagnosed with Major Depressive Disorder, 16% were diagnosed with PTSD related to the transplant, 17% evidenced symptoms of anxiety, and 6% expressed symptoms of anger-hostility. Hierarchical logistic regression analyses revealed that individuals diagnosed with PTSD during the first year post-transplant had a

13 fold increased risk for mortality at three years post-transplant. Furthermore, patients with symptoms of depression and/or anger-hostility had a four to eight fold increased risk for developing cardiac allograft disease. Medication non-adherence significantly predicted episodes of graft rejection and cardiac allograft disease. A limitation of the study is that it relied solely on patient and caregiver report of medical non-adherence, which is problematic because patients may not want to report multiple episodes of missed medication or failure to engage in recommended health behaviors (Dew et al., 1999).

Shemesh et al. (2001) employed a prospective study of PTSS and non-adherence in 140 adults who had experienced a myocardial infarction. Adult patients were followed immediately after hospitalization for myocardial infarction (n = 140) and then at six months to one year post-discharge. Patients completed one measure of PTSD (Impact of Event Scale) and one measure of general psychiatric symptoms (Symptoms Checklist-90-Revised). Adherence was assessed through pill counts of Captopril tablets. A nurse counted the patient's pills at regularly scheduled follow-up visits and compared that number to how many pills the patient would have been expected to have if the medication were taken as prescribed. Adherence was based on percentage of pills presumably taken. Medical outcome was determined by the number of "serious adverse events," identified as hospitalizations for recurrent myocardial infarction or death (Shemesh et al., 2001).

Using multiple regression analyses, results indicated that "above threshold" levels of PTSS (above threshold levels as determined by the Impact of Event Scale are correlated with a diagnosis of PTSD) were significantly correlated with patient non-adherence. Interestingly, other psychiatric symptoms, as measured by the SCL-90-R, were not associated with medication adherence. Furthermore, non-adherence was



correlated with medical outcome (“severe adverse events”) (Shemesh et al., 2001). One limitation of the study was that only “above threshold” levels of PTSD were determined by the self-report measure. Although above threshold levels are associated with a diagnosis of PTSD on this particular measure, a definitive diagnosis could not be made. In addition, although the study revealed significant associations, causality cannot be determined between PTSD and adherence (Shemesh et al., 2001).

### *Summary*

The reviewed literature on adherence in transplant populations yielded a number of interesting findings. First, the lack of a “gold standard” for measuring adherence was highlighted (Lemanek, 2003). There are few standardized measures of adherence, perhaps due to the fact that the medical protocols for various illnesses look very different. Therefore, many researchers have created or adapted measures of adherence for other illness populations to fit their own (Dew et al., 1996; Dew et al., 1999; Penkower et al., 2003). Studying and understanding adherence becomes potentially more complicated in pediatric populations where a caregiver is also a significant part of the equation and is generally responsible for medical care. Second, the literature indicates that psychological functioning is associated with medical non-adherence in transplant populations (Shemesh et al., 2001; Penkower et al., 2003). Individuals with psychiatric diagnoses were more likely to have difficulties adhering to the post-transplant regimen. Furthermore, several studies have demonstrated a correlation between non-adherence and poor medical outcome in transplant populations (Dew et al., 1999). Finally, there is some evidence to suggest that family functioning variables influence adherence behavior in transplant patients (Lurie et al., 2000; Serranno-Ikkos et al., 1998). The literature points to a need

for continuing research into the specific psychological factors in parents and families that may be associated with poor adherence and poor medical outcome in children.

### *Statement of the Problem*

The process of pediatric heart transplantation, beginning with being listed for transplant and continuing throughout the individual's life, can generate enormous stress in both children and parents. Alonzo (2000) asserted that, over time, the process of pediatric medical illness is one of "cumulative adversity," in that patients and parents are repeatedly assaulted with invasive medical procedures, time consuming medical regimens, and the looming threat of possible death. At times, this extreme stress can lead to PTSD. In fact, prior research has found that parents of medically ill children endorsed symptoms of both posttraumatic stress and psychological difficulties (Kazak et al., 1997; Manne et al., 2002; Landolt et al., 2002). For example, there is some evidence to suggest that parents of liver, kidney, and/or heart transplant patients demonstrate PTSS (Young et al., 2003).

Given these findings, one might speculate on the possible effects of parental PTSS on parents' ability to help their child adhere to the medical regimen. One study of children with a liver transplant found an association between PTSS and non-adherence to the medical regimen (Shemesh et al., 2000). A second study linked PTSS in adult myocardial infarction patients with medical non-adherence (Shemesh et al., 2001). However, there is no research on this relationship in parents of pediatric heart transplant patients.

I assert that the process of pediatric heart transplant may engender PTSS in parents and that these symptoms will affect parent's ability to help their child effectively

adhere to the enduring, complex post-transplant medical regimen. Therefore, this study will seek to understand if and how PTSS in parents affects pediatric heart transplant survivors and their subsequent medical adherence. The purpose of this study is to examine the relationships among parent psychological functioning, parenting stress, parent PTSS, medical adherence and illness severity in pediatric heart transplant patients.

The **primary hypotheses** to be tested are:

*Hypothesis 1:* Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be significantly associated with medical adherence, such that higher levels of parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with lower levels of medical adherence.

*Hypothesis 2:* Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with current transplant related illness severity, such that higher levels of parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with higher levels of transplant related illness severity.

*Hypothesis 3:* Current transplant related illness severity will be associated with levels of medical adherence, such that higher levels of transplant related illness severity will be associated with lower levels of medical adherence.

## CHAPTER III

### Method

#### *Design*

The study design was correlational and cross-sectional, using parent report questionnaire measures, cardiologist ratings, drug assays, and medical chart review.

#### *Setting*

This project was conducted in the Departments of Psychiatry and Cardiology at Children's Hospital Boston. The Pediatric Heart Transplant Team is a multidisciplinary program consisting of physicians, nurses, psychiatrists/psychologists, social workers and a variety of medical consultants.

#### *Participants*

In total, 57 participants were recruited for the study. Of those, four had missing data due to incomplete or missing questionnaires. Another parent completed the questionnaires but was removed because the child had severe developmental delay, which met a priori exclusion criteria. Therefore, the final data set was comprised of 52 participants (6 fathers and 42 mothers of different children).

The mean age of heart transplant recipients in this study was 10.81 years ( $SD = 5.33$ ), with a range of 1 to 18 years. Of the 52 children in the study, there were 30 males and 22 females, 31 with a pre-transplant diagnosis of Acquired Heart Disease and 21 with Congenital Heart Disease. The average time since transplant was 3.33 years ( $SD = 2.90$ ), with a range of one month to 10 years.

Of the 52 parents who participated in the study, 46 were female and 6 were male. Thirty-seven parents were married, 8 were single parents, 5 were divorced, 1 was separated, and 1 was in a long-term committed relationship. Parents were predominantly Caucasian/White (n = 43), followed by Hispanic (n = 4), African American (n = 2), Asian (n = 1), American Indian/Alaska Native (n = 1), and “Other” (n = 1).

### *Parent Measures*

*Brief Symptom Inventory.* The BSI (Derogatis, 1993) is a 53 item self-report measure that assesses a range of psychological symptoms (Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism). The BSI is the short form of the SCL-90-R, an assessment measure that reviews diagnostic criteria for psychological disorders. The BSI has good internal consistency reliability (Cronbach’s alpha ranges from .71-.85) and test-retest reliability (.68-.91 for nine scales and .90 for the global indices). The internal consistency for this study was excellent (Cronbach’s alpha = .95).

*Pediatric Inventory for Parents.* The PIP is a 42 item self-report measure of parenting stress associated with caring for a child with a medical illness (Streisand, Braniecki, Tercyak, & Kazak, 2001). It assesses four areas of adjustment and stress: Communication (i.e., with child and health care team), Emotional Distress (i.e., feeling helpless, seeing child sad), Medical Care (i.e., making decisions, bringing child to the clinic), and Role Function (i.e., being unable to go to work, being in the hospital). These areas are measured along two dimensions: Frequency and Difficulty. The sum of the four domains provides a total score on the two dimensions (PIP Total Frequency and PIP Total Difficulty scores). In this study, these two scores were highly correlated (.84); thus,

only the PIP Total Difficulty score was used, as it seemed most relevant to the study questions. The PIP has good internal consistency reliability (Cronbach's alpha: .80-.96) and good construct validity, in that it correlates highly with other measures of state anxiety and parenting stress. The internal consistency for this study was excellent (Cronbach's alpha = .96). The PIP is the only measure of parenting stress that specifically taps the experience of caring for a medically ill child and the unique stressors that accompany this.

*Impact of Events Scale- Revised* The IES -R is a 22 item self-report measure that assesses the three main components of post-traumatic stress disorder: intrusion, avoidance, and hyperarousal (Weiss & Marmar, 1997). The IES-R is designed to measure post-traumatic stress symptoms as defined by the DSM-IV. It asks participants to respond to questionnaire items based upon a particular life event (in this case, parents' feelings and reactions to their child's heart transplant and ongoing illness). The measure has good test-retest reliability (correlation coefficients ranging from .51 to .94, depending upon time since 1<sup>st</sup> administration/time elapsed since trauma). Furthermore, the IES has good predictive and construct validity (Weiss & Marmar, 1997). In this study, the IES showed good internal consistency (Cronbach's alpha = .91).

*Posttraumatic Diagnostic Scale:* The PDS is a 49 item self-report measure designed to assess symptoms of posttraumatic stress disorder (PTSD) (Foa, 1995). It provides a preliminary diagnosis of PTSD according to DSM-IV criteria, as well as ratings of symptom severity and level of impairment of functioning. It has good internal consistency, with an alpha of .92 for Total Symptom Severity. The internal consistency for this study was good, with an alpha of .81. Test-retest reliability of PTSD diagnosis

revealed a kappa of .74. Diagnoses of post-traumatic stress disorder at two time points indicated an agreement rate of 87%. Test-retest reliability for total PTSD score (.83 for Total Symptom Severity) was acceptable. Validity of PTSD diagnosis was examined through comparison to the Structured Clinical Interview for the DSM-IV (SCID). There was an 82% agreement rate between the PDS and the SCID (Foa, 1995).

*Recent Life Changes Questionnaire (RLCQ):* The RLCQ (Miller & Rahe, 1997) is an updated version of the Holmes-Rahe Social Readjustment Rating Scale, a measure designed to assess various life changes while providing a rating of severity of life stress (Holmes & Rahe, 1967). The measure demonstrates good internal consistency (Holmes & Rahe, 1967) and has been widely used with a variety of normative and clinical populations. The original version was recently re-scaled to incorporate life stresses that were not included in the original measure and to recalculate the degree of stress typically created by various life events. The RLCQ is a 74 item questionnaire that assigns “life change units” to stressors related to an individual’s health, work, family, personal, and financial life (Miller & Rahe, 1997). The internal consistency for this study revealed an alpha of .75.

*The Parent 24-hour Adherence Recall Measure:* This is an adaptation of a well-established measure of adherence used with diabetic patients (Johnson, Silverstein, Rosenbloom, Carter, & Gunningham, 1986; Johnson, 1993; Freund, Johnson, Silverstein, & Thomas, 1991). A similar measure has been used in other studies of adherence among pediatric transplant populations (Zelikovsky & Walsh, in press). This measure asks parents to report their child’s post-transplant regimen (i.e., medications and dosage), and then asks them to report the dosages, frequency, and time of day their child actually took

medication in the last 24 hours. It also asks questions about late or missed dosages. Additionally, there are modules that ask about clinic attendance and factors that might contribute to non-adherence (i.e., inconvenience, difficulty following regimen). The authors of the pediatric renal transplant adherence instrument are currently validating its use in transplant populations (N. Zelikovsky). Currently, no well-established assessment tool for adherence exists for this population.

For the purposes of this study, parents were considered adherent if they reported no late or missed medication dosages in the last 24 hours. Likewise, parents were placed in the non-adherent category if they reported missing or being late on one or more dosages. Therefore, the “Parent Adherence Index” was a dichotomous variable, in which a score of “0” indicated adherence and a score of “1” indicated non-adherence.

*Demographic Information Form:* This included questions about age, ethnicity, marital status, and occupation.

#### *Cardiologist/Nurse Practitioner Measures*

*Cardiologist/Nurse Practitioner Transplant Adherence Ratings.* These are a series of questions rated by the medical provider regarding the patient’s level of adherence to the post-transplant regimen. These items were generated by pediatric cardiologists, and the rating form was being developed for routine inclusion in studies of adherence in this patient population at Children’s Hospital Boston. Similar methods have been used in other populations, such as asthma (Logan, Zelikovsky, Labay, & Spergel, 2003).

A cardiologist and the primary nurse for the heart transplant team rated each patient on his or her adherence to outpatient clinic visits and the medication regimen. The “Cardiologist Adherence Index” was created; therefore, patients received a score of



“0” if they were rated as adherent to medication and clinic visits, while those whose ratings indicated some non-adherence to either medication or clinic visits received a score of “1.” There was an 85% agreement rate between the two raters.

*Pediatric Transplant Side Effect Severity Scale.* The SESS integrates the large number of medical side effects that may accompany heart transplantation into a clinically meaningful index of medical severity. The intent was to examine overall medical severity rather than the presence or absence of individual symptoms. The SESS produces a cumulative score indicating level of illness severity.

*Immunosuppressive Medication Levels (Cyclosporine and Tacrolimus):* Blood levels of these immunosuppressant medications were routinely gathered during the course of the child’s cardiac visit. Cardiologists and/or nurse practitioners identified the therapeutic drug range for each child. Cyclosporine and tacrolimus levels were generally considered out of the therapeutic range if they were below 100 ng/ml or above 250 ng/ml (Flippin, Canter, & Balzer, 2000).

#### *Chart Review*

The medical record review involved the project coordinator gathering information concerning the following in the past year: time since transplant, pre-transplant diagnosis, number of biopsies, catheterizations, clinic visits, and hospitalizations.

#### *Procedures*

At the start of the project, letters containing general information and an overview of the study were sent to all eligible families (N = 70) of heart transplant recipients. An addressed, stamped letter was enclosed so that parents could respond that they did not wish to be approached about the study. Only one parent responded that she did not wish

to be approached about the study. At the time of the child's appointment, the cardiology transplant nurse, who was quite familiar with the heart transplant families, reviewed the list of potential participants to see if any were currently experiencing a severe stressor (e.g., a medical crisis), so that they would not be approached at that time. However, no families met this criterion, and all families were approached. Twelve potentially eligible families were not seen in clinic during the time of data collection. When parents and children came to the hospital for a regularly scheduled clinic visit, the project coordinator (Lisa Farley) approached all parents except for the one who returned the "do not approach" letter. The project coordinator met with the vast majority of study participants, although a trained research assistant helped with data collection, particularly in instances when multiple patients were scheduled during a single clinic day.

The informed consent form was read and thoroughly reviewed with parents by the project coordinator or research assistant. All parents who were approached agreed to participate. Parents were asked to complete the parental psychological functioning measures (BSI, PIP, IES, PDS, and RLCQ) and 24-hour adherence recall measures during their child's appointment (when they would otherwise be waiting). Parents either completed the measures in their child's treatment room, the cardiology waiting room, or the biopsy recovery room, depending on the specific nature of their child's appointment. Completion of the instruments took approximately 30-45 minutes. Each parent received a voucher for free parking.

Within a week of the patient's visit, the cardiologist or nurse practitioner directly involved in the patient's care completed the Cardiology Ratings of Adherence and the Pediatric Transplant Side Effect Severity Scale. A chart review was performed by the

project coordinator to obtain time since transplant, pre-transplant diagnosis (congenital or cardiomyopathy), number of clinic visits, hospitalizations, catheterizations, and biopsies in the past year. Drug levels were gathered by the medical staff during the child's clinic visit through blood draws.

## CHAPTER IV

### Results

#### *Current Illness Severity*

The mean number of cardiology clinic visits during the previous one-year period was 6.17 ( $SD = 3.79$ , range = 2-16), the mean number of cardiac hospitalizations was 1.02 ( $SD = 1.50$ , range = 0-8), the mean number of cardiac catheterizations was 2.92 ( $SD = 1.80$ , range = 1-8), and the mean number of cardiac biopsies was 2.50 ( $SD = 1.35$ , range = 0-6). On the Side Effect Severity Scale, a measure completed by cardiologists/nurse practitioners to indicate the number of negative side effects and symptoms occurring post-transplant, the mean for the total number of side effects was 33.25 ( $SD = 12.55$ ). The current data differs from previous illness severity data collected on heart transplant patients at Children's Hospital Boston (DeMaso et al., 1995), in that the current sample had significantly fewer side effects ( $M = 33.25$ ,  $SD = 12.55$ ) and thus less illness severity, than previous populations of heart transplant patients ( $M = 42.22$ ,  $SD = 15.99$ ),  $t(51) = -6.30$ ,  $p < .001$ .

#### *Parental Functioning*

Measures of parental psychological functioning indicated that parents reported a significant amount of symptom distress (see Table 1). Means for the study sample were compared to means available in the literature using independent sample t tests. On a global measure of psychological distress (Global Severity Index of the Brief Symptom Inventory), the study sample ( $M = .51$ ,  $SD = .42$ ) demonstrated significantly higher symptom levels than the normative sample of adult non-patients ( $M = .30$ ,  $SD = .31$ ),  $t$

(55) = 3.54,  $p < .001$  (Derogatis, 1993). Thus, parents of pediatric heart transplant patients exhibited significant symptoms of global psychological distress.

On a measure of parenting stress related to caring for a medically ill child (PIP), the study sample had a mean of 112.40 ( $SD = 24.62$ ) on Total Frequency and a mean of 102.29 ( $SD = 26.22$ ) on the Total Difficulty score of parenting stress. Using an independent sample t-test, parents of pediatric heart transplant patients scored significantly higher than parents of oncology patients on Total Frequency,  $t(127) = 4.07$ ,  $p < .001$ , but lower on Total Difficulty,  $t(126) = -2.11$ ,  $p < .05$  (Streisand et al., 2001). Thus, the study population reported a greater number of stressful events related to caring for an ill child, but did not rate these events as being as difficult as parents of children with cancer.

On the Impact of Events Scale, a measure of post-traumatic stress symptoms, the mean for the Total score was 17.29 ( $SD = 13.68$ ), which was significantly lower than two samples of mothers of pediatric cancer survivors,  $t(160) = -3.93$ ,  $p < .001$  (Kazak et al., 2004), and  $t(123) = -2.00$ ,  $p < .05$  (Barakat et al., 1997). Hence, it appears that mothers of cancer survivors demonstrated greater trauma symptoms than the study sample. Data from the Post-Traumatic Diagnostic Scale indicated that 19% of parents of heart transplant patients met clinical criteria for post-traumatic stress disorder. In contrast, a national co-morbidity study of psychiatric diagnoses found the lifetime prevalence rate of PTSD in the general population was 7.8% (Kessler et al., 1995). Therefore, the study sample had an almost two and a half times greater rate of PTSD than the general population. When compared with a large sample of people with PTSD who had experienced various traumas (i.e., fire, sexual assault), the study sample was significantly

lower on the PDS,  $t(142) = -18.89, p < .001$  (Foa et al., 1997). However, there were no significant differences in post-traumatic stress symptoms between the study sample and mothers of children with diabetes,  $t(61) = -1.22, p = .23$  (Landolt et al., 2002), and organ transplantation,  $t(113) = -.42, p = .67$  (Young et al., 2003).

On the Recent Life Changes Questionnaire, the mean score was 274.35 ( $SD = 189.32$ ). A score of 500 or above in a one year period indicates extremely high levels of stress and risk for stress related illnesses. In the current sample, 17% of parents scored greater than 500. When compared with a large normative sample of women, participants in this study sample scored significantly higher,  $t(51) = 8.50, p < .001$  (Miller & Rahe, 1997).

**Table 1: Descriptive Statistics for Parent Psychological Functioning Variables**

<u>Variable</u>	<u>n</u>	<u>Mean</u>	<u>SD</u>	<u>Range</u>
BSI Global Severity Index	52	.51	.42	0- 1.75
PIP Total Difficulty Score	52	102.29	26.22	44- 148
IES-R Total Score	52	17.29	13.68	0- 54
PDS Symptom Severity	52	9.77	6.51	0- 25
RLCQ Total Life Change Units	52	274.35	189.32	0- 771

Note: BSI= Brief Symptom Inventory; PIP= Pediatric Inventory for Parents; IES= Impact of Event Scale; PDS = Post-Traumatic Diagnostic Scale; RLCQ= Recent Life Change Questionnaire.

Relationships among the parent psychological variables were examined through a Pearson correlation matrix. Out of 10 bivariate relationships, 8 were statistically

significant. The measure of general psychological distress (BSI) was significantly correlated with measures of parenting stress related to caring for a medically ill child (PIP) and symptoms of post-traumatic stress (IES, PDS). The difficulty of parenting stress related to caring for a medically ill child (PIP) was significantly associated with symptoms of posttraumatic stress (IES, PDS) and general life stress (RLCQ). The parent psychological questionnaires were all moderately correlated; thus, they appeared to have measured related psychological symptoms (See Table 2).

**Table 2: Pearson Correlation Matrix of Parent Psychological Variables**

<u>Variable</u>	<u>BSI</u>	<u>PIPD</u>	<u>IES</u>	<u>PDS</u>	<u>RLCQ</u>
BSI		.45*	.58**	.68**	.22
PIPD			.74**	.66**	.33*
IES				.73**	.14
PDS					.44**

Note: BSI= Brief Symptom Inventory Global Severity Scale; PIPD= Pediatric Inventory for Parents Total Difficulty Scale; IES= Impact of Event Scale Total Score; PDS = Posttraumatic Diagnostic Scale Symptom Severity Score; RLCQ= Recent Life Change Questionnaire Total Score.

\*p < .05

\*\*p < .01

### *Medical Adherence*

The adherence data yielded three different sources of information: parent report, two cardiologist ratings, and immunosuppressant drug levels. Non-adherence on the parent measure was determined by any report of non-adherence to the child's medical regimen (i.e., missed medication). Cardiologists completed two measures of patient

adherence: medication adherence and clinic appointment adherence. These two reports were combined to produce an overall index of cardiologist rated adherence. Drug levels were considered in the non-adherent category if they were out of the therapeutic range. The kappa between parent and cardiologist reports of adherence was .42 (83% agreement), while the kappa between parent report and drug levels was .13 (72% agreement). The kappa between drug levels and cardiologist report of adherence was .16 (74% agreement).

In terms of parent adherence, 42 parents (81%) reported total adherence to their post-transplant regimen, while 10 parents (19%) reported some instances of non-adherence. In the cardiologist ratings of clinic attendance, 47 parents (90%) were reported to have total adherence, while 5 parents (10%) were reported to have some non-adherence. In the cardiologist ratings of medication adherence, 44 parents (85%) were reported to have total adherence, while 8 parents (15%) were reported to have some non-adherence. When the two cardiologist ratings of clinic attendance and medication adherence were combined to produce a single index of cardiologist-rated adherence, 43 parents (83%) were in the total adherence category, while 9 parents (17%) were in the non-adherence category.

When drug levels were examined as to whether or not they were in the therapeutic range, 40 children (77%) were reported to be in therapeutic range and 10 children (19%) were reported to be out of therapeutic range. Drug assays were not taken on two of the children because it was not considered clinically indicated at the time of the visit.

Therefore, when combining all of the measures of adherence, 32 parents (62%) were considered to be adherent on all three measures, 13 parents (25%) were non-



adherent on one measure, 5 parents (9%) were non-adherent on two measures, and 2 parents (4%) were non-adherent on all three measures. Parent report, 2 cardiologist ratings, and drug levels were then combined into a single overall adherence index, such that participants who indicated non-adherence by either parent report, cardiologist report, or drug level were placed in the non-adherent group. The rationale behind this categorization was based upon the known tendency to underreport non-adherence; that is, given that parents do not always report instances of non-adherence and clinicians are not always able to detect this behavior, an index score was created that was sensitive to non-adherent behaviors. Hence, 32 parents (62%) were considered to be adherent, whereas 20 parents (38%) were non-adherent (see Table 3).

**Table 3: Descriptive Statistics for Medical Adherence**

<i>Variable</i>	<i>Total Adherence</i>	<i>NonAdherence</i>
Parent Rated Adherence	81%	19%
Cardiologist Clinic Rated Adherence	90%	10%
Cardiologist Medication Rated Adherence	85%	15%
Cardiologist Adherence Index (Combination of Clinic and Medication Ratings)	83%	17%
Drug Levels	77%	19%
Overall Adherence Index	62%	38%

*Primary Hypotheses and Analyses:*

*Hypothesis 1:* Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be significantly associated with medical adherence, such that higher levels of parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with lower levels of medical adherence.

*Univariate Analyses of Parent Psychological Variables and Adherence:*

Univariate analyses were conducted to compare parent and child demographic characteristics and parental psychological functioning variables for parents in the adherence group versus the non-adherence group. Dichotomous variables such as gender were compared using the chi-square test, and continuous variables such as age were compared with the two-sample t test. As noted in Tables 4 and 5, the univariate analyses indicated that demographic and psychological variables did not significantly differ when broken down into adherent and non-adherent groups.

**Table 4: Univariate Analyses for Demographic Characteristics by Adherence Index**

<u>Variable</u>	<u>Adherent</u>	<u>Non-Adherent</u>	<u>t value or chi sq</u>	<u>p value</u>
Child Gender				
Male	20 (62.5%)	10 (50.0%)	.79	.38
Female	12 (37.5%)	10 (50.0%)		
Parent Gender				
Male	2 (6.3%)	4 (20.0%)	2.30	.13
Female	30 (93.8%)	16 (80.0%)		
Child's Age	10.72 (4.85)	10.95 (6.13)	-.14	.89

Note: Child and Parent Gender are reported with the number and percent. Child's age is reported with mean and standard deviation.

**Table 5: Univariate Analyses for Parent Psychological Variables by Adherence Index**

<u>Variable</u>	<u>Adherent</u>		<u>Non-Adherent</u>		<u>t value</u>	<u>p value</u>	<u>Effect Size</u>
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>			
BSI GSI	.43	.28	.64	.57	-1.55	.13	.49
PIPD	104.59	25.78	98.60	27.15	.79	.43	.23
IES	17.66	14.12	16.70	13.27	.25	.81	.07
PDS	10.06	6.10	9.30	7.31	.40	.69	.11
RLCQ	281.94	180.34	262.20	207.11	.35	.72	.10

Note: BSI = Global Severity Index of Brief Symptom Inventory; PIPD = Pediatric Inventory for Parents Difficulty Total; IES = Impact of Events Total; PDS = Post-traumatic Diagnostic Scale Total Severity; RLCQ = Recent Life Changes Questionnaire Total.

It is possible that significant differences between the groups were not found due to the relatively small size of the study sample. Therefore, effect sizes were calculated to determine differences possibly obscured by the low sample size. Effect size represents the degree of an independent variable's effect on the dependent variable (Grimm & Yarnold, 1995). The BSI Global Severity Index yielded a medium effect size (.49), indicating that the non-adherent group may have experienced greater psychological distress than the adherent group.

Because there were no significant differences between the adherent and non-adherent groups on any of the parent psychological functioning variables, multivariate regression analyses were not conducted. Hence, Hypothesis 1 was partially confirmed in that there was a moderate effect size demonstrated between the adherent and non-adherent groups on a global index of psychological distress.

*Hypothesis 2:* Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with current transplant related illness severity, such that higher levels of parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with higher levels of transplant related illness severity.

*Univariate Analyses of Parent Psychological Functioning Variables and Illness Severity:*

Pearson correlation coefficients were calculated to measure the magnitude of the relationship between parent psychological functioning measures (BSI, PIP, IES, PDS, RLCQ) and transplant-related illness severity (SESS). All measures yielded continuous variables. Results indicated that the parent psychological variables did not significantly correlate with the illness severity measure (see Table 6).

**Table 6: Pearson Correlation Matrix of Parent Psychological Variables and Illness Severity**

<u>Variable</u>	<u>RLCQ</u>	<u>BSI</u>	<u>PIPD</u>	<u>IES</u>	<u>PDS</u>
SESS	.06	.10	.11	.10	.02
p value	.67	.50	.44	.46	.92

Note: SESS = Pediatric Transplant Side Effect Severity Scale; RLCQ = Recent Life Change Questionnaire; BSI = Brief Symptom Inventory; PIPD = Pediatric Inventory for Parents Difficulty Total; IES = Impact of Event Scale; PDS = Posttraumatic Diagnostic Scale.

There were no significant correlations between the parent psychological functioning variables and illness severity. Therefore, multivariate regression analyses were not conducted. Hence, Hypothesis 2 was not confirmed.

*Hypothesis 3:* Current transplant related illness severity will be associated with levels of medical adherence, such that higher levels of transplant related illness severity will be associated with lower levels of medical adherence.

*Univariate Analyses of Illness Severity and Adherence:*

Univariate analyses were conducted to compare the illness severity variables for parents in the adherent and non-adherent groups (see Table 7).

**Table 7: Univariate Analyses for Illness Severity by Adherence Index**

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<u>Variable</u>	<u>Adherent</u>	<u>Non-Adherent</u>	<u>t value</u>	<u>p value</u>
Cumulative Side Effects	33.34 (12.37)	33.10 (13.16)	.07	.95
Cardiac Biopsies	2.56 (1.52)	2.40 (1.05)	.46	.65
Catheterizations	3.16 (2.13)	2.55 (1.10)	1.37	.18
Clinic Visits	6.56 (3.84)	5.55 (3.72)	.94	.35
Hospitalizations	.91 (1.15)	1.20 (1.96)	-.61	.55

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There were no significant differences between the adherent and non-adherent groups on any of the illness severity variables. Therefore, multivariate regression analyses were not conducted. Hence, Hypothesis 3 was not confirmed.

*Summary:*

Therefore, results indicated that parents of children who have undergone heart transplantation reported significant psychological distress. They experienced higher levels of global psychological symptoms than a sample of normative adults. When compared with parents of oncology patients, the study sample reported more instances of parenting stress, but rated these experiences as less difficult. Furthermore, parents of heart transplant patients demonstrated significantly higher rates of PTSD when compared with rates reported in the general population. When compared with other illness populations on the severity of PTSD symptoms, study parents were similar to parents of children with diabetes and other organ transplants, while they experienced lower symptom levels than parents of cancer survivors and other adults with varying traumatic

experiences diagnosed with PTSD (i.e., sexual assault). Study parents also reported high levels of general life stress, which were significantly higher than the normative population.

The first hypothesis postulated a relationship between parent psychological variables and non-adherence. While 38% of the study population indicated some form of non-adherence to the medical regimen, adherence was not significantly related to parental psychological variables. However, a moderate effect size was found between the adherent and non-adherent groups on a global index of psychological distress and functioning. The second hypothesis, asserting a relationship between parent psychological symptoms and illness severity, was not confirmed. Likewise, the final hypothesis examining the relationship between illness severity and medical adherence was not confirmed.

## CHAPTER V

### Discussion

In this chapter, the results from the present study will be reviewed and compared with findings in the research literature. The hypotheses will be further explored and possible explanations for the findings examined. Finally, limitations of the study as well as implications for practice and research will be reviewed.

#### Illness Severity

When compared with data collected from pediatric heart transplant patients in 1995 and 1998 (DeMaso et al.), the current sample of pediatric heart transplant patients had significantly fewer illness related side effects. One would expect this to be the case, as the treatment and management of transplant-related side effects continues to improve. The dosing and types of immunosuppressant medications are continually being modified and tested so that patients experience the positive effects of the medication (i.e., body's defenses will not reject the new heart), while minimizing the negative consequences often brought on by treatment (i.e., susceptibility to infection). Treatments for post-transplant management have improved dramatically over the last ten years; thus, it is reasonable to expect that current populations of transplant patients are experiencing better health and fewer side effects than even transplant patients of several years ago. Nevertheless, the data indicated that current patients continue to experience a number of negative side effects as a result of their illness and treatment, including hypertension, renal insufficiency, and infection.



## Parent Psychological Symptoms

### *Global Psychological Distress and General Life stress*

Overall, the results indicated that parents of pediatric heart transplant patients experienced significant psychological symptoms, general life stress, and parenting stress related to their child's heart condition. For instance, on a measure of global psychological distress, the study sample reported significantly more psychological symptoms, as well as a higher intensity of distress, than a non-clinical adult population. On a measure of general life stress, 17% reported a high frequency of life events that put them at significant risk for stress related illnesses.

### *Parenting Stress*

Parents reported a number of symptoms of stress specifically related to caring for a medically ill child. Areas of concern involved communication (speaking with the medical staff about the child's illness), medical care (making decisions about child's medical care), role function (attending to other life issues while dealing with child's illness), and emotional distress (managing the emotional sequelae related to caring for an ill child). When compared with parents of pediatric oncology patients, the study sample reported a higher *frequency* of stressful events related to taking care of a medically ill child, while parents of oncology patients rated stressful events as more *difficult* to manage than did the study population. It is unclear as to why these differences might exist. One hypothesis is that the post-transplant regimen tends to be more chronic and requires consistent lifetime follow-up, whereas oncology treatment might be more acute and intensive during a discrete period of time.

The measure of parenting stress used in the study (PIP) is relatively new; therefore, there is little other data with which to compare the current sample. However, as opposed to general measures of parenting stress, this measure provided unique insight into the particular stresses parents encounter in caring for an ill child. In fact, many parents reported that this measure was the most useful and truly seemed to tap into their experience. Many stated that they identified with the questionnaire items and “saw themselves” reflected in them. Indeed, parents endorsed a wide variety of stresses unique to parenting an ill child.

#### *Post-Traumatic Stress Symptoms*

Parents in the study sample reported symptoms of post-traumatic stress in response to their child’s heart transplant. Results indicated that 19% of parents met DSM-IV diagnostic criteria for post-traumatic stress disorder, almost two and a half times greater than the lifetime prevalence rate in the general population (Kessler et al., 1995). The presence of post-traumatic stress symptoms in parents has been documented in a number of pediatric illnesses, such as cancer (Stuber et al., 1996; Barakat et al., 1997), diabetes (Landolt et al., 2002), and solid organ transplant (Young et al., 2003). The present findings are consistent with previous research on PTSD in parents of chronically ill children (Best et al., 2001; Kazak et al., 1997) and lend support to the hypothesis that pediatric chronic illness, in this case heart transplantation, can be conceptualized as a traumatic event for parents.

These findings are consistent with Alonzo’s (2000) stipulation that PTSD and PTSS (Post-Traumatic Stress Symptoms) develop as a result of the cumulative nature of the traumas associated with chronic illness (i.e., invasive medical procedures). In this

framework, having a child undergo a heart transplant can be viewed as a traumatogenic experience. For instance, the most obvious trauma would be the actual surgery, although the continued stress associated with fear of rejection, multiple medical appointments, and hospitalizations constitute smaller traumas that produce an additive effect. For instance, during the time of data collection, several children died while either waiting for transplant or as a result of complications post-transplant. While the study parents were not on the inpatient unit at the time they completed the study, many were aware of these events. These types of experiences are frequently difficult for parents, and over time might gradually wear at their emotional defenses. In this way, it is helpful to view PTSS as Alonzo (2000) suggests, as a continuum on which repeated traumatization might lead one towards sub-clinical symptoms or a diagnosis of PTSD.

The present study documented the level of psychological distress experienced by parents of transplant patients, in terms of general psychological symptoms, the stresses of daily living, and the difficulties associated with caring for a medically ill child. Most notably, however, is the finding that many parents reported symptoms of post-traumatic stress that they associated with their ongoing experience of caring for a child with a heart transplant. The research literature has found that a diagnosis of PTSD is associated with increased rates of depression, substance abuse, and an overall impairment in functioning (American Psychiatric Association, 1994). With 19% of study parents meeting full criteria for post-traumatic stress disorder, this study highlights the need for appropriate identification and treatment referrals for parents in this population.

## Medical Adherence

Medical adherence was measured in three ways: parent 24 hour recall of medical regimen, cardiologist ratings of medication and clinic adherence, and blood levels of immunosuppressant medication. Each of these indicators of adherence produced roughly the same number of individuals in the non-adherent category: parent report indicated 19% non-adherence, total cardiologist index demonstrated 17% non-adherence, and drug levels indicated 19% non-adherence. There was not perfect agreement among parent, cardiologist, or drug level reports; each assessment method identified slightly different non-adherent individuals.

Given that previous literature has documented the tendency for adherence to be underreported (Rapoff, 1999), parents were considered non-adherent on an overall index if one of the above measures indicated non-adherent behavior. Thus, results on the overall index indicated that 38% of parents were non-adherent to their child's medical regimen, as indicated by either ratings by cardiologists, immunosuppressant drug levels, or their own report.

This is generally consistent, if somewhat higher than, previous research findings on adherence in pediatric renal transplants (21% non-adherence), heart and heart-lung transplants (30% non-adherence), and heart transplants (40% non-adherence) (Blowey et al., 1997; Serranno-Ikkos et al., 1998; Ringewald et al., 2001). However, the studies used for comparison with the study sample defined adherence using varying methodologies, thus making comparisons with the study population less reliable. For example, primary methods of measuring adherence in other studies included using electronic monitoring caps (which record the date and time the medication bottle was opened), blood levels of

cyclosporine (immunosuppressant), medical staff “estimation” of adherence, and the use of medical diaries. Often, cut-off points were established for sufficient adherence; however, this is difficult to compare across studies given the different populations and the varying lengths of time over which adherence was assessed.

Despite the fact that the majority of study parents were completely adherent (62%), the data suggests that non-adherence is a problem for a substantial subset of heart transplant patients and their parents. It is important to note, however, that this data may underestimate the actual amount of non-adherent behaviors in this population. During data collection, several parents expressed hesitancy to report an instance of missed or late medication, despite assurances by the investigator that the data was confidential and would not be revealed to the cardiology staff. Also, parents were asked to recall medication adherence in the 24 hours prior to their current outpatient visit. It is possible that medication adherence was higher on those days when parents knew their child would be attending a medical appointment and drug levels would be checked. Finally, data was collected only from those parents who attended clinic visits. Based upon general clinic data and practitioner report, two to four out of approximately fifty clinic visits per month are missed. It is reasonable to hypothesize that non-adherence might be greater in patients who failed to attend regularly scheduled clinic visits, thus creating a potential underestimation of non-adherent behaviors.

Hypothesis 1: Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be significantly associated with medical adherence, such that higher levels of parental psychological distress, illness related parenting stress, and

post-traumatic stress symptoms will be associated with lower levels of medical adherence.

This hypothesis was partially confirmed. Although the relationship between global psychological distress and medical adherence was not significant, the effect size was moderate, suggesting that parents who were distressed were less likely to be adherent. Therefore, this finding suggests that parents who are struggling with a number of psychological symptoms might have difficulty managing the chronic demands of their child's medical regimen.

Other measures of parent psychological symptoms were not, however, significantly related to medical non-adherence. There are several possible reasons as to why a relationship was not found between non-adherence and the other psychological measures. The rationale behind the hypothesis was that parents who were traumatized by their child's heart transplant and experiencing psychological distress might find it difficult to adhere to a complex medical regimen. The postulate was that this distress would interfere with functioning in a way that might negatively impact the child's post-transplant follow up. Thus, although 19% of parents met diagnostic criteria for PTSD, symptoms of parental post-traumatic stress did not appear to be related to the manner or degree to which their child adheres to his or her medication regimen or outpatient appointments.

It is possible that instead of negatively influencing adherence, symptoms of post-traumatic stress, such as hyper-vigilance, actually contribute to "following doctor's orders" in some cases. For instance, a parent who is traumatized by a child's heart transplant might be anxious about *not* following the medical protocol for fear of the

consequences to the health of their child. Some traumatized parents may be more attuned and acutely aware that failure to take medications might lead to serious and possibly life threatening rejection of the transplanted heart. Other parents might simply not allow for PTSD symptoms to affect their child's medical care. In many ways, this finding points to the resiliency and adaptability on the part of parents. The results suggest that although some parents of pediatric heart transplant patients may be traumatized, they are still largely able to adhere to their child's post-transplant regimen.

Hypothesis 2: Parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with current transplant related illness severity, such that higher levels of parental psychological distress, illness related parenting stress, and post-traumatic stress symptoms will be associated with higher levels of transplant related illness severity.

This hypothesis was not confirmed. Consistent with the first hypothesis, parental distress did not appear to compromise the child's degree of illness severity. Conversely, the magnitude of a child's illness was not associated with parental psychological health. This finding challenges a commonly held clinical assumption by health care providers that parents of very ill children are more likely to be traumatized or in distress. Similarly, DeMaso et al. (1991) reported that pediatric cardiac patient's degree of illness severity was not correlated with their emotional status. The present study extended DeMaso et al.'s findings to parents of heart transplant patients.

One possible reason for this finding is that there was little variation in illness severity in the current population. The children in the study were all being seen at the Heart Transplant Clinic on an outpatient basis. Therefore, despite being post-transplant,

all of the children were well enough to be managed by clinic visits, and were considered healthy enough to engage in daily activities. Perhaps there would have been variation in levels of parental distress if the sample had included children who were hospitalized or had at-home nursing care, as this would represent higher illness severity and a disruption in quality of life.

It is also possible that parental psychological functioning is not significantly influenced by a child's illness severity, but rather by other factors such as perceptions of the child's illness and expectations following transplant, attitudes towards medical treatment, social support, and/or hope about the child's future. Therefore, one might speculate that it is the coping style and cognitive assumptions made on the part of parents that influence their psychological response to transplant, rather than objective data on the severity of their child's illness. Further research is needed to elucidate the specific factors that contribute to parental adaptation post-transplant.

Hypothesis 3: Current transplant related illness severity will be associated with levels of medical adherence, such that higher levels of transplant related illness severity will be associated with lower levels of medical adherence.

No relationship was found between illness severity and medical adherence, which is contrary to previous research that found an association between non-adherence and episodes of rejection (Ringewald et al., 2001; Shemesh et al., 2001). However, Shemesh et al. (2001) examined the adherence-rejection relationship in a sample of adult cardiac patients; it is possible that adult patients have more complicating medical factors and age related effects (i.e., diabetes, high blood pressure, osteoporosis) that affected the rate of



rejection and mortality found in the study. These confounding variables may not have been as influential or relevant in a pediatric population.

Furthermore, the hypothesis may not have been confirmed in the current sample because of measurement issues related to adherence. Adherence was measured at one time point, thus providing a snapshot of the patient's current behavior. There may not have been enough information to provide a strong enough association between adherence behaviors gleaned from one day and the severity of the child's post-transplant illness. Examining patients' adherence behaviors over time might have increased the likelihood of finding a significant relationship between non-adherence and severity of the illness.

Finally, it is important to note that clinically there is not always a linear relationship between medical adherence and the child's level of illness related side effects. For reasons that are often unclear, a child and parent may be perfectly adherent to the medical regimen, but nevertheless have a poor medical outcome. Alternatively, mediocre or poor adherence, particularly if short-lived, may not necessarily lead to negative medical symptoms. This may explain why a significant relationship was not found between illness severity and medical adherence in the current study.

### Summary

In summary, parents of pediatric heart transplant patients reported a number of psychological symptoms, including global psychological distress, general life stress, parenting stress, and post-traumatic stress symptoms. Difficulties with adherence were reported in 38% of the study population, although adherence was not significantly associated with parent psychological functioning or illness severity. However, a moderate effect size was found for the relationship between global psychological

functioning and medical adherence. There was not a significant relationship between parent psychological functioning and child's level of illness severity.

### Limitations

There are several limitations to consider when interpreting the results of this study. The sample consisted of predominantly Caucasian families in the Northeastern United States, thus limiting the generalizability of the sample. Additionally, the sample size is relatively small, despite the fact that it is one of the larger samples found in the literature on parents of pediatric heart transplant patients. Nevertheless, the sample size may have made it more difficult to detect statistically significant differences between the groups.

It is important to note that there was likely a sampling bias inherent in the study, thus creating a restricted range from which the sample was chosen. First, the study sample included patients recruited from the outpatient clinic. Thus, heart transplant patients who were hospitalized and/or too ill to be seen in the outpatient clinic did not participate in the study. It is possible that adherence and parental psychological functioning variables might differ between hospitalized and outpatient populations. Furthermore, several patients died during the course of data collection. Therefore, the most severely ill children were not included in the study sample. Finally, families with adherence difficulties may have been identified during the pre-transplant evaluation. In these cases, the heart transplant team may not have allowed for transplantation in part due to significant concerns about medical follow-up. Therefore, the study sample was selected from families who had already met criteria for transplant, including endorsement

by the medical team that they would be adherent to the post-transplant regimen. These aforementioned factors likely resulted in a restricted range for subject sampling.

Another potential limitation of the study was the exclusive use of self-report measures in assessing parent diagnoses of PTSD. The Post-Traumatic Diagnostic Scale provided a provisional diagnosis of PTSD based upon the clinical criteria stipulated in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). However, a structured diagnostic interview might produce a more accurate and precise assessment of parents in the clinically significant range.

Finally, the measurement of adherence was a limitation of the study. Research has repeatedly shown that adherence remains a somewhat elusive and difficult concept to capture, despite multiple assessment strategies (Rapoff, 1999). In fact, there is no “gold standard” specified by the research literature (Lemanek, 2003). The present study attempted to examine adherence through the use of multiple informants and measurement techniques. Different perspectives were gained through 24-hour parent recall, cardiologist ratings of medication and clinic adherence, and measurement for appropriate levels of immunosuppressant drug levels. All of these assessment tools helped to identify various non-adherent behaviors in the study population.

Despite the multiple avenues through which adherence was studied, limitations existed with each strategy. The parent recall measure asked parents to report their child’s adherence to the post-transplant regimen in the last 24 hours. It is possible that parents were more likely to be adherent when they knew that their child would be coming to clinic and getting their blood levels drawn. This may have increased the likelihood that adherence levels would be inflated. Additionally, social desirability factors might have

influenced parents' responses. Parents are repeatedly told by the medical team that adherence to the medical regimen is crucial to their child's survival. Despite multiple assurances by the study investigator that individual responses would not be viewed by the medical team, some parents may have felt embarrassed or anxious to admit to not following medical advice. This may have made decreased the likelihood of accurate reporting.

The cardiology staff rated each patient on their level of adherence to taking necessary medications and attending clinic appointments. While the staff maintains regular contact with patients and are quite familiar with their medical needs, they are not able to consistently observe all behaviors and make definitive conclusions about a patient's level of adherence. Thus, the cardiology staff's rating represents a subjective clinical judgment and not an objective conclusion.

Drug assays are routinely used to monitor the level of medication in a patient's blood to ensure that it stays within a specified therapeutic range. Generally, if a patient is not taking medication as prescribed, it can be identified through blood work. However, it is possible to have a "false positive," in that drug levels may be out of the therapeutic range due to other factors besides non-adherence (i.e., interaction effects with other medication).

Despite multiple measurement techniques, it is difficult to encapsulate the construct of adherence, in part because it likely changes over time and is somewhat difficult to operationalize and measure. Additionally, adherence behaviors may wax and wane, depending upon life circumstances and the degree to which the medical regimen interferes with an individual's daily activities and quality of life. The challenge of future

research lies in refining the methods by which we measure adherence and possibly developing new strategies that better capture this construct.

### Implications for Clinical Practice

As technology improves and medications become more advanced, the number of heart transplants performed will continue to increase. Approximately 260 pediatric heart transplants occur in the United States each year (Blume, 2003), with a five year survival rate of approximately 75% (Boucek et al, 2002). Thus, increasing importance is placed on research that investigates factors that improve medical and psychosocial outcomes.

Findings from the current research study have several important implications. First, parents of children who have undergone a heart transplant are at risk for significant psychological distress, including clinical levels of post-traumatic stress that exceed rates in normative populations. They experienced high levels of parenting stress surrounding caring for a medically ill child. Therefore, it would be important for transplant teams to identify parents who are demonstrating psychological impairment. Transplant teams generally include mental health professionals, such as psychologists, psychiatrists, and social workers. With the knowledge that parents in this population are at risk for these difficulties, it would be advisable for the transplant team to take a proactive, preventive approach, both clinically and in future research studies. This could include offering parent support groups, psychoeducational programs for both parents and physicians, and psychological follow-up as a routine part of the standard of care post-transplant.

Even prior to the transplant, the importance of adherence is evident for the study population. For instance, in the pre-transplant evaluation, consideration is given to

whether or not a family has been adherent to the child's current treatment regimen. Reservations about conducting the transplant are raised if the staff are worried that the family environment is not stable enough to manage the stress of transplant follow-up. In this study, 38% of parents demonstrated some sort of non-adherent behavior to their child's post-transplant regimen. Similar to other populations of pediatric chronic illnesses, the participants in this sample also struggled with maintaining the high level of day-to-day medical care necessary to keep their child healthy. For this reason, early intervention might be key in helping to support at-risk families and to increase adherence behaviors. Additionally, regular check-ins with medical staff might be important in the early stages of the transplant to help identify potential problems. Medical staff and researchers alike need to continue to look for ways to increase adherence behaviors and intervene effectively when parents are having difficulty.

#### Implications for Future Research

The present study yielded many interesting findings into the nature of psychological distress experienced by parents of pediatric heart transplant patients and how these symptoms are associated with illness severity and medical adherence. A substantial subset of parents of pediatric heart transplant patients experienced Post-Traumatic Stress Disorder and general psychiatric symptoms. However, this study is among the first to examine PTSD in this population; relatively little is known about the correlates and outcomes of PTSD in parents of transplant patients. Future studies might examine predictors of PTSD, including factors that make an individual more susceptible to these difficulties in the wake of a child's heart transplant. Research is needed that

examines how psychiatric diagnoses, and PTSD in particular, influence the family system, attachment, and parent-child functioning.

While parental traumatization was not found to significantly influence adherence behaviors, it may be that PTSS impact different aspects of parents' lives that were not examined in this study, such as interpersonal relationships or occupational functioning. Additionally, studies that investigate parental coping and adjustment with a child's ongoing illness would prove helpful. Research is needed that elucidates the specific mechanisms that facilitate adaptive parent psychological functioning.

A recent paper highlighted a relatively new concept in the literature referred to as "posttraumatic growth," which is defined as "the cognitive process by which those who have experienced trauma apply positive interpretations to and find meaning in the traumatic event" (Barakat, Alderfer, & Kazak, 2005, pg. 2). This introduces a new focus in the PTSD literature; in addition to investigating pathological symptoms that interfere with functioning, this concept emphasizes the potential for growth in the midst of difficult circumstances. For instance, in a study of adolescent survivors of cancer and their parents, Barakat et al. (2005) found that approximately 90% of mothers and 80% of fathers identified positive growth resulting from the experience of their child's cancer. Changes included more positive feelings about their life, how they treat others, and how they view the future.

This new study on post-traumatic growth is applicable to the findings and future directions associated with the current study in several ways. First, the present study identified parents in the clinically diagnostic range of PTSD at an almost two and a half times greater rate than the lifetime prevalence in the general population (Kessler et al.,

1995). Despite this, however, the results indicated that these symptoms did not influence their child's level of illness severity or parents' ability to help their child adhere to the medical regimen. This perhaps highlights resiliency factors and coping resources that influence the outcome of parental PTSD. In addition to examining the negative outcomes of PTSD, future research might investigate the ways in which parents grow and make sense of their child's life-threatening illness. Furthermore, it would be interesting to examine those factors that facilitate post-traumatic growth in families; this would provide a broader framework in which to understand medical trauma, as well as a point of intervention for clinical staff.

The present study suggested that parents of heart transplant patients experience difficulties with adherence. Further studies on adherence in this population are crucial, specifically regarding those factors that influence and promote adherent behavior, such as communication and relationship with the medical team, social support, and attitudes towards transplant. Questions on the interactive effects of parent and child attitudes towards adherence need further examination. The current study found a moderate effect size suggesting that only the most severe parental psychopathology was associated with non-adherent behavior. Replication of these findings and continued investigation would be helpful in further understanding the correlates and specific nature of these relationships.

Furthermore, the study design was cross-sectional, and thus did not allow for examinations into causal relationships and changes in parental psychopathology and non-adherence over time. Therefore, longitudinal research is necessary in order to answer questions about the development of PTSD and other psychiatric symptoms in parents



following heart transplant. Important information could be gathered on how non-adherent behaviors develop or change from immediately after surgery to several years post-transplant. Temporal relationships between parental psychological functioning, illness severity, and medical adherence would provide greater insight into the complexity of factors that influence post-transplant care.

The sample size for this study was among the largest found in the literature on parents of heart transplant patients. Although the rate of pediatric transplantation is increasing, it remains a relatively low incidence phenomenon. However, in order to gain a sample size sufficient for more complex and sophisticated statistical methods, multi-site studies at several transplant centers across the country would be important.

Finally, preventive intervention and treatment protocols to help facilitate mental health and positive coping following transplant need to be developed and tested. The ultimate hope is to develop effective interventions that allow both parents and pediatric patients to feel supported and equipped with the necessary skills to embark upon the rare and complex journey they must negotiate after heart transplantation.

## References

- Alonzo, A. (2000). The experience of chronic illness and post-traumatic stress disorder: The consequences of cumulative adversity. *Social Science and Medicine, 50*, 1475-1484.
- American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition*. Washington, DC.
- Barakat, L.P., Alderfer, M.A., & Kazak, A.E. (2005). Posttraumatic growth in adolescent survivors of cancer and their mothers and fathers. *Journal of Pediatric Psychology, 1-7*.
- Barakat, L.P., Kazak, A.E., Meadows, A.T., Casey, R., Meeske, K., & Stuber, M.L. (1997). Families surviving childhood cancer: A comparison of posttraumatic stress symptoms with families of healthy children. *Journal of Pediatric Psychology, 22*, 843-859.
- Barakat, L.P., Kazak, A.E., Gallagher, P.R., Meeske, K., & Stuber, M. (2000). Posttraumatic stress symptoms and stressful life events predict the long-term adjustment of survivors of childhood cancer and their mothers. *Journal of Clinical Psychology in Medical Settings, 7* (4), 189-196.
- Becker, M.H. & Maiman, L.A. (1975). Sociobehavioral determinants of compliance with health and medical care recommendations. *Medical Care, 13*, 10-24.
- Bennett-Johnson, S. (1993). Chronic diseases of childhood: Assessing compliance with

- complex medical regimens. In N.A. Krasnegor, L. Epstein, S. Bennett-Johnson & S.J. Yaffe (Eds.), *Developmental Aspects of Health Compliance Behavior*. New Jersey: Lawrence Erlbaum Associates.
- Best, M., Streisand, R., Catania, L., & Kazak, A.E. (2001). Parental distress during pediatric leukemia and posttraumatic stress symptoms after treatment ends. *Journal of Pediatric Psychology*, 26 (5), 299-307.
- Blowey, D.L., Hebert, D., Arbus, G.S., Pool, R., Korus, M., & Koren, G. (1997). Compliance with cyclosporine in adolescent renal transplant recipients. *Pediatric Nephrology*, 11, 547-551.
- Blume, E.D. (2003). Current status of heart transplantation in children: update 2003. *Pediatric Clinics of North America*, 50, 1375-1391.
- Boucek, M.M., Edwards, L.B., Keck, B.M., Trulock, E.P., Taylor, D.O., & Mohacsi, P.J. (2002). The registry of the International Society for Heart and Lung Transplantation: fifth official pediatric report: 2001-2002. *Journal of Heart and Lung Transplant*, 21, 827-840.
- Briere, J. (1997). *Psychological assessment of adult posttraumatic states*. Washington DC: American Psychological Association.
- Brownbridge, G., & Fielding, D.M. (1994). Psychosocial adjustment and adherence to dialysis treatment regimens. *Pediatric Nephrology*, 8, 744-749.
- Campis, L.B., DeMaso, D.R., & Twente, A.W. (1994). The role of maternal factors in the adaptation of children with craniofacial disfigurement. *Cleft Palate-Craniofacial Journal*, 32 (1), 55-61.
- Chinnock, R.E. (2002). Heart transplantation. *eMedicine Journal* 2002.

Retrieved [April 15, 2004] from the World Wide Web:

<http://www.emedicine.com/ped/topic 2797.htm>.

Cimato, T.R. & Jessup, M. (2002). Recipient selection in cardiac transplantation: contraindications and risk factors for mortality. *Journal of Heart Lung Transplant, 21* (11), 1161-1173.

Davis, C.C., Brown, R.T., Bakeman, R., & Campbell, R. (1998). Psychological adaptation and adjustment of mothers of children with congenital heart disease: Stress, coping, and family functioning. *Journal of Pediatric Psychology, 23* (4), 219-228.

Dahlquist, L.M., Czyzewski, D.I., & Jones, C.L. (1996). Parents of children with cancer: A longitudinal study of emotional distress, coping style, and marital adjustment two and twenty months after diagnosis. *Journal of Pediatric Psychology, 21* (4), 541-554.

DeMaso, D.R. (2001). Pediatric Heart Disease. In R.T. Brown (Ed.), *Handbook of Pediatric Psychology in School Settings*. New Jersey: Lawrence Erlbaum Associates, Inc.

DeMaso, D.R., Campis, L.K., Wypij, D., Bertram, S., Lipshitz, M., & Freed, M. (1991). The impact of maternal perceptions and medical severity on the adjustment of children with congenital heart disease. *Journal of Pediatric Psychology, 16*, 137-149.

DeMaso, D.R., Kelley, S.D., Bastardi, H., O'Brien, P., & Blume, E. (2004). The

- longitudinal impact of psychological functioning, medical severity, and family functioning in pediatric heart transplantation. *Journal of Heart and Lung Transplantation*, 23 (4), 473-480.
- DeMaso, D.R., Twente, A.W., Spratt, E.G., O'Brien, P. (1995). The impact of psychological functioning, medical severity, and family functioning in pediatric heart transplantation. *Journal of Heart and Lung Transplantation*, 14, 1102-1108.
- Derogatis, L.R. (1993). *Brief Symptom Inventory: Administration, Scoring, and Procedures Manual (4<sup>th</sup> Edition)*. Minneapolis, MN: NCS Pearson, Inc.
- Dew, M.A., Kormos, R.L., DiMartini, A.F., Switzer, G.E., Schulberg, H.C., Roth, L.H., & Griffith, B.P. (2001). Prevalence and risk of depression and anxiety-related disorders during the first three years after heart transplantation. *Psychosomatics*, 42 (4), 300-313.
- Dew, M.A., Kormos, R.L., Roth, L.H., Murali, S., DiMartini, A., & Griffith, B.P. (1999). Early post-transplant medical compliance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *Journal of Heart and Lung Transplantation*, 18 (6), 549-562.
- Dew, M.A., Roth, L.H., Thompson, M.E., Kormos, R.L., & Griffith, B.P. (1996). Medical compliance and its predictors in the first year after heart transplantation. *Journal of Heart and Lung Transplantation*, 15 (6), 631-644.
- Dunbar-Jacob, J., Erlen, J.A., Schlenk, E.A., Ryan, C.M., Sereika, S.M., & Doswell, W.M. (2000). Adherence in chronic disease. *Annual Review of Nursing Research*, 18, 48-90.
- Epstein, L.H. & Cluss, P.A. (1982). A behavioral medicine perspective on

- adherence to long-term medical regimens. *Journal of Consulting & Clinical Psychology, 57*, 950-971.
- Flippin, M.S., Canter, C.E., & Balzer, D.T. (2000). Increased morbidity and high variability of cyclosporine levels in pediatric heart transplant recipients. *Journal of Heart and Lung Transplantation, 19* (4), 343-349.
- Foa, E. (1995). *Posttraumatic Stress Diagnostic Scale: Manual*. Minneapolis, MN: National Computer Systems.
- Foa, E.B., Cashman, L., Jaycox, L., & Perry, K. (1997). The validation of a self-report measure for posttraumatic stress disorder: The posttraumatic diagnostic scale. *Psychological Assessment, 9*, 445-451.
- Foulkes, L.M., Boggs, S.R., Fennell, R.S., Sibinski, K. (1993). Social support, family variables, and compliance in renal transplant children. *Pediatric Nephrology, 7*, 185-188.
- Freund, A., Johnson, S.B., Silverstein, J., & Thomas, J. (1991). Assessing daily management of childhood diabetes using 24-hour recall interviews: Reliability and stability. *Health Psychology, 10* (3), 200-208.
- Fricker, F.J., Addonizio, L., Bernstein, D., Boucek, M., Canter, C., Chinnock, R., Chin, C., Kichuk, M., Lamour, J., Pietra, B., Morrow, R., Rotundo, K., Shaddy, R., Schuette, E., Schowengerds, K.O., Sondheimer, H., & Webber, S. (1999). Heart transplantation in children: Indications. *Pediatric Transplantation, 3*, 333-342.
- Glover, D.A. & Poland, R.E. (2002). Urinary cortisol and catecholamines in

mothers of child cancer survivors with and without PTSD.

*Psychoneuroendocrinology*, 27, 805-819.

Haynes, R.B. (1979). Introduction. In R.B. Haynes, D.W. Taylor, & D.C.

Sackett (Eds.), *Compliance in health care*. Baltimore: The Johns Hopkins University Press.

Hoekstra-Weebers, J.E., Jaspers, J., Kamps, W.A., & Klip, E.C. (1999). Risk

factors for psychological maladjustment of parents of children with cancer.

*Journal of the American Academy of Child and Adolescent Psychiatry*, 38 (12), 1526-1535.

Hoekstra-Weebers, J.E., Jaspers, J., Kamps, W.A., & Klip, E.C. (2001).

Psychological adaptation and social support of parents of pediatric cancer patients: A prospective longitudinal study. *Journal of Pediatric Psychology*, 26 (4), 225-235.

Holmes, T.H. & Rahe, R.H. (1967). The social readjustment rating scale. *Journal of Psychosomatic Research*, 11, 213-218.

Holmbeck, G.N., Gorey-Ferguson, L., Hudson, T., Seefeldt, T., Shapera, W.,

Turner, T., & Uhler, J. (1997). Maternal, paternal, and marital functioning in families of preadolescents with spina bifida. *Journal of Pediatric Psychology*, 22 (2), 167-181.

Johnson, S.B., Silverstein, J., Rosenbloom, A., Carter, R., & Cunningham, W.

(1986). Assessing daily management of childhood diabetes. *Health Psychology*, 5, 545-564.

Kazak, A.E. & Barakat, L.P. (1997). Brief report: Parenting stress and quality of

life during treatment for childhood leukemia predicts child and parent adjustment after treatment ends. *Journal of Pediatric Psychology*, 22 (5), 749-758.

Kazak, A.E., Barakat, L.P., Meeske, K., Christakis, D., Meadows, A.T., Casey, R., Penati, B., & Stuber, M.L. (1997). Posttraumatic stress, family functioning, and social support in survivors of childhood leukemia and their mothers and fathers. *Journal of Consulting and Clinical Psychology*, 65 (1), 120-129.

Kazak, A.E., Stuber, M.L., Barakat, L.P., Meeske, K., Guthrie, D., & Meadows, A.T. (1998). Predicting posttraumatic stress symptoms in mothers and fathers of survivors of childhood cancers. *Journal of the American Academy of Child and Adolescent Psychiatry*, 37 (8), 823-831.

Kirklín, J.K., Young, J.B., McGiffin, D.C., & Shumway, N.E. (2002). *Heart Transplantation* New York: Churchill Livingstone.

Kupst, M.J., Natta, M.B., Richardson, C.C., Schulman, J.L., Lavigne, J.V., & Das, L. (1995). Family coping with pediatric leukemia: Ten years after treatment. *Journal of Pediatric Psychology*, 20 (5), 601-617.

LaGreca, A.M., Follansbee, D., & Skyler, J.S. (1990). Developmental and behavioral aspects of diabetes management in youngsters. *Children's Health Care*, 19, 132-139.

LaGreca, A.M. & Schuman, W.B. (1995). Adherence to prescribed medical regimens. In M.C. Roberts (Ed.) *Handbook of pediatric psychology* (2<sup>nd</sup> Ed.). New York: Guilford.

Landolt, M.A., Ribí, K., Laimbacher, J., Vollrath, M., Gnehm, H.E., &



- Sennhauser, F.H. (2002). Brief report: Posttraumatic stress disorder in parents of children with newly diagnosed type 1 diabetes. *Journal of Pediatric Psychology*, 27 (7), 647-652.
- Lemanek, K.L. (2003). Adherence. In M.C. Roberts (Ed.), *Handbook of Pediatric Psychology*. New York: The Guilford Press.
- Logan, D., Zelikovsky, N., Labay, L., & Spergel, J. (2003). The illness management survey: Identifying adolescents' perceptions of barriers to adherence. *Journal of Pediatric Psychology*, 28 (6), 383-392.
- Lurie, S., Shemesh, E., Sheiner, P.A., Emre, S., Tindle, H.L., Melchionna, L., & Schneider, B.L. (2000). Non-adherence in pediatric liver transplant recipients: An assessment of risk factors and natural history. *Pediatric Transplantation*, 4 (3), 200.
- Manne, S.L., DuHamel, K., Gallelli, K., Sorgen, K., & Redd, W.H. (1998). Posttraumatic stress disorder among mothers of pediatric cancer survivors: Diagnosis, comorbidity, and utility of the PTSD checklist as a screening instrument. *Journal of Pediatric Psychology*, 23 (6), 357-366.
- Manne, S., DuHamel, K., Nereo, N., Ostroff, J., Parsons, S., Martini, R., Williams, S., Mee, L., Sexson, S., Wu, L., Difede, J., & Redd, W.H. (2002). Predictors of PTSD in mothers of children undergoing bone marrow transplantation: The role of cognitive and social processes. *Journal of Pediatric Psychology*, 27 (7), 607-617.
- Meyers, K.E., Thomson, P.D., & Weiland, H. (1996). Noncompliance in children and adolescents after renal transplantation. *Transplantation*, 62, 186-189.

- Miller, M.A. & Rahe, R.H. (1997). Life changes scaling for the 1990s. *Journal of Psychosomatic Research*, 43 (3), 279-292.
- O'Neill, L., & D'Angelo, E. (1986). A study of the surgical decision-making process of parents who have infants with a congenital heart defect. In E.F. Doyle, M.A. Engle, W.M. Gersony, W.J. Rashkind, & N.S. Talner (Eds.), *Pediatric Cardiology*. New York: Springer-Verlag.
- Penkower, L., Dew, M.A., Ellis, D., Sereika, S.M., Kitutu, J.M., & Shapiro, R. (2003). Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients. *American Journal of Transplantation*, 3 (11), 1418.
- Rapoff, M.A. (1999). *Adherence to Pediatric Medical Regimens*. New York: Plenum Publishers.
- Rapoff, M.A. & Barnard, M.U. (1991). Compliance with pediatric medical regimens. In J.A. Cramer & B. Spilker (Eds.), *Patient compliance in medical practice and clinical trials*. New York: Raven Press.
- Ringewald, J., Gidding, S.S., Crawford, S.E., Backer, C.L., Mavroudis, C., & Pahl, E. (2001). Nonadherence is associated with late rejection in pediatric heart transplant patients. *The Journal of Pediatrics*, 139 (1), 75-78.
- Sawyer, M.G., Streiner, D.L., Antoniou, G., Toogood, I., & Rice, M. (1998). Influence of parental and family adjustment on the later psychological adjustment of children treated for cancer. *Journal of the American Academy of Child and Adolescent Psychiatry*, 37 (8), 815-822.
- Serano -Ikkos, E., Lask, B., & Whitehead, B. (1997). Psychosocial morbidity in

- children and their families awaiting heart or heart-lung transplantation. *Journal of Psychosomatic Research*, 42 (3), 253-260.
- Serrano-Ikkos, E., Lask, B., & Whitehead, B. (1998). Incomplete adherence after pediatric heart and heart-lung transplantation. *Journal of Heart and Lung Transplantation*, 17 (12), 1177-1183.
- Serrano-Ikkos, E., Lask, B., Whitehead, B., Rees, P., Graham, P. (1999). Heart or heart-lung transplantation: Psychosocial outcome. *Pediatric Transplantation*, 3, 301-308.
- Shaw, R.J., Palmer, L., Blasey, C., & Sarwal, M. A typology of non-adherence in pediatric renal transplant recipients. *Pediatric Transplantation*, 7, 489-493.
- Shemesh, E., Lurie, S., Stuber, M.L., Emre, S., Patel, Y., Pankaj, V., Aromando, M., & Shneider, B. (2000). A pilot study of posttraumatic stress and nonadherence in pediatric liver transplant recipients. *Pediatrics*, 105 (2), 29.
- Shemesh, E. Rudnick, A., Kaluski, E., Milovanov, O., Salah, A., Alon, D., Dinur, I., Blatt, A., Metzkor, M., Golik, A., Verd, Z., & Cotter, G. (2001). A prospective study of posttraumatic stress symptoms and nonadherence in survivors of a myocardial infarction. *General Hospital Psychiatry*, 23 (4), 215-222.
- Sloper, P. (2000). Predictors of distress in parents of children with cancer: A prospective study. *Journal of Pediatric Psychology*, 25 (2), 79-91.
- Streisand, R., Braniecki, S., Tercyak, K., & Kazak, A. (2001). Childhood illness-related parenting stress: The Pediatric Inventory for Parents. *Journal of Pediatric Psychology*, 26 (3), 155-162.
- Streisand, R., Rodrigue, J.R., Houck, C., Graham-Pole, J., & Berlant, N. (2000).

- Brief report: Parents of children undergoing bone marrow transplantation: Documenting stress and piloting a psychological intervention program. *Journal of Pediatric Psychology*, 25 (5), 331-337.
- Stuber, M.L., Christakis, D.A., Houskamp, B., & Kazak, A.E. (1996). Posttrauma symptoms in childhood leukemia survivors and their parents. *Psychosomatics*, 37, 254-261.
- Stukas, A.A., Dew, M.A., Switzer, G.E., DiMartini, A., Kormos, R.L., & Griffith, B.P. (1999). PTSD in heart transplant recipients and their primary family caregivers. *Psychosomatics*, 40 (3), 212-221.
- Thompson, R.J. & Gustafson, K.E. (1996). Psychological adjustment of parents and siblings. In R.J. Thompson & K.E. Gustafson (Eds.), *Adaptation to Chronic Childhood Illness*. Washington, DC: American Psychological Association.
- Thompson, R.J. & Gustafson, K.E. (1996). Adherence. In R.J. Thompson & K.E. Gustafson (Eds.), *Adaptation to Chronic Childhood Illness*. Washington, DC: American Psychological Association.
- Todaro, J.F., Fennell, E.B., Sears, S.F., Rodrigue, J.R., & Roche, A.K. (2000). Review: Cognitive and psychological outcomes in pediatric heart transplantation. *Journal of Pediatric Psychology*, 25 (8), 567-576.
- Van Horn, M., DeMaso, D.R., Gonzalez-Heydrich, J., & Erickson, J.D. (2001). Illness-related concerns of mothers of children with congenital heart disease. *Journal of the American Academy of Child and Adolescent Psychiatry*, 40 (7), 847-854.
- Weiss, D. & Marmar, C. (1997). The Impact of Event Scale-Revised. In J.

Wilson & T. Keane (Eds.), *Assessing psychological trauma and PTSD*. New York: Guilford.

Wynn, K.S., & Eckel, E.M. (1986). Juvenile rheumatoid arthritis and home physical therapy program compliance. *Physical & Occupational Therapy in Pediatrics, 6*, 55-63.

Young, G.S., Mintzer, L.L., Seacord, D., Castaneda, M., Mesrkhani, V., & Stuber, M.L. (2003). Symptoms of posttraumatic stress disorder in parents of transplant recipients: Incidence, severity, and related factors. *Pediatrics, 111* (6), 725-731.

Zelikovsky, N. & Walsh, A. (in press). Adherence to medical regimens. In B.S. Kaplan & K.E. Meyers (Eds.), *Requisite in Pediatrics: Nephrology/Urology*. St Louis, MO: Harcourt Health Sciences.

