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Predictors Of Immunosuppressant Adherence In Long-term Renal Transplant Recipients

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PREDICTORS OF IMMUNOSUPPRESSANT ADHERENCE IN LONG-TERM RENAL TRANSPLANT RECIPIENTS

by

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ABSTRACT

To sustain the health and viability of renal transplants, adherence to immunosuppressant therapy (IST) medications is critical. Studies continue to identify decreased adherence rates as time from transplant increases (Chisholm-Burns, Kwong, Mulloy & Spivey, 2008; Chisholm, Lance, Mulloy, 2005; Chisholm, Mulloy, & DiPiro, 2005; Nivens & Thomas, 2009). While previous research has explored the effect of variables known to influence IST adherence in adult renal transplant recipients, limited studies have explored these variables in a population of renal transplant recipients with longer time posttransplant intervals. The purpose of this study was to examine demographic variables, time posttransplant, immunosuppressive agents, health beliefs, social support, and symptom experience and test their relationship to adherence in a population of long-term renal transplant recipients.

A cross-sectional correlational design was used to collect data from a convenience sample of 98 adult renal transplant recipients who were three or more years from transplant. Participants completed five instruments: 1) demographic survey, 2) the Beliefs About Medicines Questionnaire (BMQ), 3) the Medical Outcomes Study (MOS) Modified Social Support Survey (MSSS), 4) the Basel Assessment of Adherence with Immunosuppressive Medication Scales (BAASIS), and 5) the Modified Transplant Symptom Occurrence and Symptom Distress Scale-59R (MTSOSD-59R). A composite adherence score (CAS) consisting of a self-report measure of adherence (BAASIS), nontherapeutic serum drug assay, and collateral report of adherence as provided by two transplant clinic professionals was used to determine final adherence group classification (adherent/nonadherent). Analysis of the relationship between all independent variables and adherence was conducted using Spearman's rho correlation coefficient. Mean scores for medication complexity, health beliefs, social support, and symptom experience were

compared between age, gender, and time posttransplant groups using independent-samples *t* tests. A logistic regression prediction of probability was conducted to determine which of the variables that demonstrated a significant relationship to adherence were most predictive of adherence.

Of the total sample population ($N = 98$), 39.8% ($n = 39$) were classified as adherent and 60.2% ($n = 59$) were nonadherent. Results demonstrated no significant relationship between age (continuous variable), time posttransplant, immunosuppressant medications (measured by a medication complexity index), health beliefs, symptom experience, and adherence. Weak, but significant relationships between age groups ($r = -.213$, p=.035), tangible social support ($r = .215$, $p = .017$), emotional informational social support ($r = .274$, $p = .003$), positive social interaction support ($r = .199$, $p = .025$), total overall social support ($r = .274$, $p = .003$) and composite adherence group classification were found. Older participants ($\geq$ 55 yrs) were significantly less adherent than younger ($\leq$ 54 yrs) participants. Mean scores for emotional / informational (EMI), positive social interaction (POS), and total social support (MSSS) were significantly lower in nonadherent participants. Regression results indicated the overall model of two predictors (age grouped [$\leq$ 54 yrs; $\geq$ 55 yrs] and EMI social support subscale) was statistically reliable in distinguishing between adherent and nonadherent participants (-2 Log Likelihood 116.244; Goodness-of-Fit x^2 (2) = 13.664, $p = .001$), correctly classifying 69.1% of the cases.

Findings from this study contribute to the body of research exploring predictors of immunosuppressant adherence in long-term renal transplant recipients. Data suggest both younger age ($\leq$ 55) and categories of social support predict adherence in long-term renal transplant recipients. Healthcare providers caring for renal transplant recipients long-term

should consider annually assessing older participants for adherence as well as for changes in social networks.

This dissertation is dedicated to my husband Michael and son Jacob. Without their unwavering support, encouragement, and patience, I could not have gone the distance.

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CHAPTER ONE: INTRODUCTION

The Problem

To sustain the health and viability of renal transplants, adherence to a lifelong regimen of immunosuppressant therapy (IST) is critical. Within the adult renal transplant population, nonadherence to IST medications has been identified as contributing substantially to increased risk of both acute and late acute rejection as well as increased graft loss with odds of graft failure increasing in recipients identified as nonadherent (Butler, Roderick, Mullee, Mason, & Peveler, 2004; Nevins & Thomas, 2009). In addition, studies continue to identify decreased adherence rates as time posttransplant increases (Chisholm-Burns, Kwong, Mulloy & Spivey, 2008; Chisholm, Lance, Mulloy, 2005; Chisholm, Mulloy, & DiPiro, 2005; Nivens & Thomas, 2009). While advances in medicine and the development of more effective IST regimens have resulted in one year survival rates that exceed 90%, efforts continue to focus on reducing the incidence of acute rejection and improving long-term outcomes (United States Renal Data Systems [USRDS], 2010). Given the association of increased time posttransplant with IST nonadherence, exploration of factors that contribute to long-term IST adherence is warranted if long-term renal transplant outcomes are to improve.

Background

Within the adult renal transplant population, IST nonadherence rates vary widely (8%-65%) with an average self-reported nonadherence rate of 28% (Denhaerynck, et al. 2005). A more recent meta-analysis exploring rates of nonadherence across adult solid organ transplant

recipients concluded immunosuppressant nonadherence to be highest in renal transplant recipients (36%); the rate was more than twice the rate observed in heart recipients, and over five times greater than liver recipients (Dew et al. 2007). In addition, individual medical costs associated with persistent low adherence increased individual 3 year medical costs by over $12,000 (Pinsky et al. 2009).

Nonadherence with IST therapy is identified as contributing substantially to a median 36% (14%-65%) of graft loss (Butler, Roderick, Mullee, Mason, & Peveler, 2004). In a retrospective cohort study of 15,525 renal transplant recipients, the incidence of graft failure was 11.5% in recipients identified as poorly adherent (Pinsky, et al. 2009). Even minor deviations in IST dosing schedules have been associated with the development of adverse outcomes and graft rejection (Nevins & Thomas, 2009; Nevins, Kruse, Skeans, & Thomas, 2001; Schäfer-Keller, Lyon, Van-Gelder, & De Geest, 2006). In a retrospective analysis of IST dose reduction and discontinuation, dose reductions greater than 50% were associated with an increased hazard of graft loss while dose discontinuation resulted in an 8-fold increase in graft loss (Takemoto, Pinsky, Schnitzler, Lentine, Willoughby, Burroughs, & Bunnapradist, 2007).

The World Health Organization (WHO, 2003) in defining adherence, captured the multidimensional nature of the concept. Categories of influencing variables included in the definition were socioeconomic, patient-related, condition-related, therapy-related, and healthcare system/healthcare team-related variables. All categories of variables have been explored within the adult renal transplant population.

Of the therapy-related variables known to influence IST adherence, increased time from transplant has been a factor in IST nonadherence across the majority of studies (Chisholm-Burns,

Kwong, Mulloy, & Spivey, 2008; Chisholm, Mulloy, & DiPiro, 2005; Chisholm, Vollenweider, Mulloy, Jagadeesan, Wynn, Rogers, et al., 2000; Ichimaru, Kakuta, Okumi, Imamura, Isaka, Nonomra, Kojima, Okuyama, & Takahara, 2008; Nevins & Thomas, 2009; Vasquez, Tanzi, Benedetti, & Pollak, 2003). While substantial nonadherence with a single IST medication (18%) has been identified as early as one month following discharge (Nevins, Kruse, Skeans, & Thomas, 2001), persistent reductions in mean adherence rates for the same IST medication has been found to continue up to four years following initial transplant, supporting results obtained in earlier studies (Nevins & Thomas, 2009). In addition, one isolated study classified time posttransplant in quartiles. Authors concluded quartile 1 ($\leq$ 4 years posttransplant) as being significantly associated with higher adherence and noted for every year of increase in time posttranplant, adherence decreased by 0.3% (Chisholm-Burns, et al. 2008). Increased time posttransplant remains a nonmodifiable therapy-related factor associated with increased risk of nonadherence to IST medications.

Other variables identified as influencing adherence-immunosuppressant therapy, beliefs about medicines, social support, and symptom experience- have been explored in a few recent studies. In addition, studies exploring these variables include sample populations with recipients as early as six months to two years posttransplant. ***To date, no study*** has explored these variables ***in a group of renal transplant recipients identified as "long-term***" yielding support for exploration ***in a more long-term*** population.

Statement of Problem

Despite the performance of over 16,000 kidney transplants in 2010, over 96,000 patients currently await renal transplantation in the United States (United Network for Organ Sharing [UNOS], 2009). Given the current shortage of available organs, efforts continue to focus on improving long-term outcomes. While previous research has explored the effect of all categories of influencing variables on IST adherence in adult renal transplant recipients, limited studies have explored these variables in a population of renal transplant recipients with longer time posttransplant intervals.

Study Purpose/Aim

The purpose of this study was to examine demographic variables, time posttransplant, immunosuppressive agents, health beliefs, social support, and symptom experience and test their relationship to adherence based upon the Health Decision Model (Eraker, Becker, Strecher, & Kirscht, 1984).

Definition of Terms

Table 1 summarizes key terms as defined and operationalized in this study.

Table 1 Definition of Terms

Term	Theoretical Definition	Operational Definition
Age	Age of the participant in years at the time of study enrollment. Younger = ≤ 54 years; older = ≥ 55 years of age.	Date of birth as measured by a demographic questionnaire. Age in years at the time of study enrollment was calculated using date of study enrollment and date of birth.
Long-Term	Long-term was defined as three or more years from transplant.	Long-term was defined by the date of initial transplant as measured by a demographic questionnaire.
Time Posttransplant	Time posttransplant was defined as the total number of years since the patient's date of renal transplantation.	Time posttransplant was measured by a demographic questionnaire. Time posttransplant in years was calculated using both the date of study enrollment and the date of renal transplantation.
Immunosuppressive Agents	Immunosuppressive agents were defined as the names of medication the patient is taking for the purpose of immunosuppression.	Immunosuppressive agents were identified by a demographic questionnaire and included the medication names. Medication complexity was measured using a calculated medication complexity index-the product of the total number of IST medications, number of pills taken per day, and the number of times per day taking medications.
Health Beliefs	Health beliefs were defined as personal convictions that influence individual health behaviors (Moorhead, Johnson, Maas, & Swanson, 2008).	Health beliefs were measured by the Beliefs about Medicines Questionnaire [BMQ) (Horne, Weinman, & Hankins, 1999). Possible scores for both BMQ subscales range from five to 25 with higher scores indicating stronger beliefs.

Term	Theoretical Definition	Operational Definition
Social Support	Social support was defined as the existence or availability of a person or network of people that rely, care, and love an individual and on whom that same individual can rely (Sarason, Levine, Basham, & Sarason, 1983).	Social support was measured by the 18 item Medical Outcomes Study (MOS) Modified Social Support Survey (MSSS) subscales and total instrument scores (Sherbourne & Stewart, 1991) The18 items represent the multiple dimensions of social support-tangible, affectionate, emotional / information, positive social interaction. Possible scores range from 0-100 with higher scores indicating greater perceived support.
Symptom Experience	Symptom experience was defined as both symptom occurrence representing the cognitive component of the frequency, severity and duration of symptoms, and distress representing the emotional burden that results (Kugler, Geyer, Gottlieg, Simon, Haverich, & Dracup 2009).	Symptom experience was measured by the Modified Transplant Symptom Occurrence and Symptom Distress Scale (MTSOSD-59R) (Dobbels, Moons, Abraham, Larsen, Dupont & De Geest, 2008). Ridit scores were calculated to rank order symptom occurrence and symptom distress. Overall individual symptom occurrence and symptom distress ridit scores were compared.
Immunosuppressant Nonadherence	Immunosuppressant nonadherence was defined as "deviation from the prescribed medication regimen sufficient to influence adversely the regimen's intended effect" (Fine, Becker, De Geest, Eisen, Ettenger, et al., 2009, p. 36).	Immunosuppressant nonadherence was measured as a composite adherence score that consisted of self-reported nonadherence as scored on the Basel Assessment of Adherence with Immunosuppressive Medications Scale (BAASIS), collateral-reported nonadherence of two clinicians, and nontherapeutic assay variability. Participants were classified as adherent or nonadherent.

Research Question and Hypotheses

Based on the Health Decision Model and review of the literature, the primary research question to be addressed was which of six predictor variables-demographic variables, time posttransplant, immunosuppressive agents, health beliefs, social support, and symptom experience-are most influential in predicting IST adherence in long-term adult renal transplant recipients? The following hypotheses were tested in this study:

Hypothesis 1

There will be a significant negative relationship between the predictor variable of time posttransplant as measured in years and composite adherence group classification.

Hypothesis 2

There will be a significant relationship between the predictor variable of age as measured in years and composite adherence group classifications.

Hypothesis 3

There will be a significant relationship between medication (IST) complexity index scores and composite adherence group classifications.

Hypothesis 4

There will be a significant difference in IST complexity index scores between composite adherence group classifications.

Hypothesis 5

There will be a significant relationship between the predictor variable of health beliefs as measured by BMQ Necessity and BMQ Concerns subscale scores and composite adherence group classifications.

Hypothesis 6

There will be a significant difference in BMQ Necessity subscale, BMQ Concerns subscale, and BMQ Necessity/Concerns differential scores between composite adherence group classifications.

Hypothesis 7

There will be a significant positive relationship between the predictor variable of social support as measured by total MSSS scores and composite adherence group classifications.

Hypothesis 8

There will be a significant difference in MSSS subscale and total scale scores between composite adherence group classifications.

Hypothesis 9

There will be a significant negative relationship between the predictor variable of symptom experience as measured by MTSOSD-59R total ridit scores and composite adherence group classifications.

Hypothesis 10

There will be a significant difference in MTSOSD-59R total ridit scores between composite adherence group classifications.

Study Significance

As time posttransplant increases, follow-up care shifts from the acute care phase provided by transplant clinics during the first year following transplantation to long-term health promotion and maintenance provided by primary healthcare providers outside of the transplant clinic setting. Having an understanding of the modifiable factors that contribute to successful long term IST adherence can guide practitioners in developing and implementing appropriate interventions to sustain long- term IST adherence improving long-term graft outcomes.

Nonadherence with immunosuppressive medication in the adult renal transplant population impacts the health and viability of graft outcomes due to a variety of influencing factors. As the focus shifts to improving long-term graft outcomes, comprehensive exploration of risk factors for adherence in long-term populations helps delineate risk profiles. Research regarding the influence of risk factors for nonadherence in long-term renal transplant populations has yet to be conducted and this study will add to the current body of knowledge. Chapter 2 provides a review of literature relevant to the problem under study, illustrates the framework that guided the study, and identifies gaps in the literature to be addressed by the current study. Chapter 3 addresses methods used to carry out the research, while Chapters 4 and 5 present findings, discuss conclusions, and outline recommendations for future research.

CHAPTER TWO: LITERATURE REVIEW

To determine the state of the science of IST adherence research within the adult renal transplant population, a review of Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and PsychInfo databases was conducted using the key search terms of *adherence, immunosuppressant*, *medication,* and *renal transplant*. Secondary searches were conducted from the reference lists of selected articles. While all studies selected were published in the English language, priority was given to studies that were published within the last 10 years. Works older than 10 years considered seminal studies were included in the review. Studies that explored variables within European populations were included if literature on the variable under study was limited. Examination of previous research regarding IST adherence definition and measurement, prevalence and outcomes, and categories of determinants identified gaps in the current body of knowledge to be addressed by the proposed study.

Defining Adherence

While medication adherence rates of 80% are often cited as acceptable across many illness categories (Osterberg & Blaschke, 2005), a consensus definition of what constitutes optimum adherence in adult renal transplant recipients remains elusive. The lack of a clinically meaningful definition of adherence prevents both the identification of the degree of adherence necessary to achieve desired pharmacological effects, and the degree of subclinical nonadherence that increases the risk of adverse outcomes (acute rejection, graft loss). In light of the lack of a clinically meaningful definition of adherence, researchers have frequently dichotomized

adherence into an "all or nothing" phenomenon (adherent, nonadherent). Lost in the dichotomization of the concept of adherence are the dimensions of medication taking (taking, timing, drug holidays, and dose reductions) that contribute to the multidimensional nature of the phenomenon.

While multiple studies exploring the prevalence of IST nonadherence in adult renal transplant recipients have selected 80% adherence as the degree distinguishing adherers from nonadherers (Chisholm, Lance, & Mulloy, 2005; Chisholm, et al., 2000; Hilbrands, Hoitsma, & Koene, 1995), the majority of prevalence studies have operationalized IST nonadherence as the quantity and frequency of missed doses as measured using self-report (De Geest et al., 1995; Denhaerynck et al., 2006; Frazier, Davis-Ali, & Dahl, 1994; Ghods, Nasrollahzadeh, & Argani, 2003; Hardstaff, Green, & Talbot, 2003; Raiz, Kilty, Henry, & Ferguson, 1999; Teixeira de Barros & Cabrita, 2000; Vasquez, Tanzi, Benedetti, & Pollak, 2003). A meta-analysis of 36 studies by Butler, Roderick, Mullee, Mason, and Peveler (2004) identified the most common definition of nonadherence as missing, forgetting, or altering of a dose at least once per month. Further complicating formulation of a consensus definition is a lack of clarification of what constitutes a "late" or "missed" dose. While a few studies have defined the timing associated with a "late" dose as being ingested 2 to 2.5 hours beyond the scheduled time (Schmid-Mohler, Thut, Wüthrich, Denhaerynck, & De Geest, 2010; Sketris, Waite, Grobler, West, & Gerus, 1994; Teixeira de Barros & Cabrita, 2000), no studies to date conducted with the adult renal transplant population have explored clinician and/or patient conceptualizations of a "missed" dose.

The phenomenon of nonadherence has been described using four characteristics: timing, frequency, origin, and certainty of diagnosis (Chapman, 2004; Hansen, Seifeldin, & Noe, 2007).

Mirroring the six patterns of medication adherence noted among other chronic illness categories (Osterberg & Blaschke, 2005) occasional nonadherence has been further delineated into three subcategories: patients having near perfect adherence, patients adherent to nearly all doses but with timing irregularities, and patients missing an occasional dose. *Intermittent nonadherence* was defined further as patients taking drug holidays 3-4 times yearly. *Persistent nonadherers* were further defined as patients taking drug holidays monthly or more often, and *complete nonadherers* were identified as patients taking few or no doses of immunosuppressants (Hansen, et al., 2007). In addition, Hansen et al. (2007) defined the diagnostic certainty of nonadherence as definite (direct admission of nonadherence by patient), probable, possible or unlikely, depending upon the evaluation method.

A seminal study conducted by Greenstein and Siegal (2000), identified three profiles of nonadherent patients. *Accidental nonadherers*, accounted for the majority of nonadherence in the study population (47%) and included patients who simply forgot to take IST medications. *Invulnerable nonadherers*, accounted for 28% of the study population and included renal transplant recipients guided by the belief they do not need to take their medications regularly. *Decisive nonadherers*, those patients who employed independent decision making habits ignoring the need for medications, accounted for 25% of the sample population.

Recent studies have attempted to more clearly capture the dimensions of medication adherence behaviors. A longitudinal study by Russell et al. (2006) of 44 adult renal transplant recipients identified four patterns of IST adherence: 1) taking medications on time, 2) taking medications on time with late / missed doses, 3) rarely taking medications on time, and 4) taking medications morning and/or evening doses late, and those who missed doses. A prospective

cohort study conducted by Denhaerynck et al. (2007) captured similar patterns of nonadherence while studying the prevalence of IST nonadherence in 249 adult renal transplant recipients by exploring the percentage of taking adherence (number of prescribed doses), dosing adherence (days with correct dosing), timing adherence (taken within 25% of prescribed intervals), and drug holidays. With the advent of more self-report adherence instruments measuring all dimensions of medication taking-timing, taking, drug holidays (missed, omitted) and dose reduction-more studies exploring determinants of adherence are capturing the entire nature of the concept.

Current scholarly activities conducted within the transplant population have worked toward the formulation of solutions to address issues of definition and measurement in IST adherence research. A more succinct definition of nonadherence, intended to better represent the dynamic nature of a patient's medication taking behavior, emerged during a consensus conference on nonadherence to immunosuppressant medications (Fine, Becker, De Geest, Eisen, Ettenger et al, 2009). Understanding that satisfactory adherence results when gaps between dosing history and the prescribed regimen have no effect on clinical outcomes, experts have conceptually defined nonadherence as "***deviation from the prescribed medication regimen sufficient to influence adversely the regimen's intended effect***" (Fine et al, 2009, p. 36.).

Measuring Adherence

IST adherence studies have used both direct and indirect methods of measurement, each with identifiable limitations. Direct monitoring methods (direct observation of intake, blood /

urine biological drug assays, biological markers), have the disadvantage of being inconvenient to the patient, influenced by increased adherence prior to sampling, affected by variations in individual metabolism, and at times, prone to lab error (Chisholm, 2002; Hansen, et al. 2007). Assays obtained for medications with a short half-life may only provide information about patterns of adherence over the prior few days with no information regarding long-term adherence. In addition, therapeutic monitoring of IST medications such as mycophenolate mofetil (Cellcept) requires multiple blood samples during dosing intervals leading to increased costs, patient inconvenience, and limited feasibility across clinical settings (Jeong & Kaplan, 2007). Indirect measurement methods (patient self-report, collateral reports, prescription refill rates, pill counts, electronic drug monitoring, health outcomes), while often more simple and feasible, are not without disadvantages. Patients often under report nonadherence, prescription refill rates fail to provide information related to characteristics of nonadherence; pill counts fail to consider multiple sources of medication; and electronic monitoring fails to prove ingestion (Chisholm, 2002; Hansen, et al. 2007).

Electronic monitoring, frequently considered the gold standard measure of adherence, has limitations that challenge both internal and external measurement validity. A study by Denhaerynck et al. (2008) examined assumptions needed for internal and external validity of electronic monitoring measurement. The study tested validity through evaluation of: 1) correct functioning of electronic monitoring equipment, 2) correspondence of cap openings with actual dose intake, and 3) the influence of electronic monitoring on a patient's normal adherence behavior. Several assumptions of internal and external validity were not satisfied: 1) equipment or cap malfunctions, 2) self-reported mismatches between cap openings and drug intake in 62%

of patients, and 3) adherence decreased over 5 weeks indicating an intervention effect of the measurement method (Denhaerynck et al., 2008).

Despite the increased use of electronic monitoring, the majority of studies continue to rely heavily on self-report measures of adherence (surveys, questionnaires, interviews) (Brown et al., 2009; De Geest et al., 1995; Denhaerynck et al. 2007; Frazier et al. 1994; Ghods et al. 2003; Goldfarb-Rumyantzev, Wright, Ragasa, Ostler, Van Orden, Smith et al., 2011; Greenstein & Siegal, 1998; Kalil, Heim-Duthoy, & Kasiske, 1992; Nevins & Thomas, 2009; Raiz et al. 1999; Sharma, Gupta, Tolani, Rathi, & Gupta, 2000; Sketris, Waite, Grobler, West, & Gerus, 1994; Teixeira de Barros & Cabrita, 2000; Vasquez, Tanzi, Benedetti, & Pollak, 2003). Though prone to response bias and criticized for providing little insight into adherence characteristics, self--report measures of adherence are recognized as the most feasible method of monitoring adherence (Butler, Peveler, Roderick, Horne, & Mason, 2004). A study comparing self-report adherence with electronic measurement concluded that self-report adherence, conducted in the setting of a confidential interview, to be the better measure for detecting missed doses and erratic dose timing (Butler, et al. 2004). In addition, a recent meta-analysis of 147 studies conducted within the solid organ transplant populations concluded self-report assessments of adherence to yield the highest rates of nonadherence (Dew et al. 2007).

To date, no measure of adherence (direct, indirect) has emerged as a gold standard. Current literature supports the use of a combination of measurement methods to increase diagnostic accuracy of subclinical nonadherence (Butler, et al. 2004; Schäfer-Keller, Steiger, Bock, Denhaerynck, & De Geest, 2008). A recent study exploring the diagnostic accuracy of current IST adherence measurement methods identified a composite score composed of

information obtained from patient self-report and/or clinician collateral reports, and/or nontherapeutic assay results as having the highest sensitivity to nonadherence (72.1%) (Schäfer-Keller, et al. 2008). While specificity of the same composite score was low, evidence supports continued use of the composite score as a screening measure. Given the identified limitations associated with current methods of measurement, the continued use of measures of self-report as one component of assessing subclinical nonadherence is supported.

Prevalence and Outcomes of Nonadherence

Variations in definition and measurement prevent accurate representation of both the prevalence of IST nonadherence and the effect of IST nonadherence on clinical outcomes. The majority of studies attempt to demonstrate the effect of IST nonadherence on the clinical outcomes of acute and/or late rejection and graft failure and/or loss. A few isolated studies focusing on economic outcomes have explored with impact of IST nonadherence on healthcare costs.

Advances in immunosuppression have reduced the incidence of acute rejection episodes in the first year following transplantation (Denhaerynck et al. 2009). Despite the decrease in acute rejection rates, significant improvements have not occurred in long-term graft survival (Meier-Kriesche, Schold, Srinivas, & Kaplan, 2004). Early allograft damage, attributed to episodes of acute rejection, contributes to the development of chronic allograft nephropathy (chronic rejection) (Pascual, Theruvath, Kawai, Tolkoff-Rubin, & Cosimi, 2002). Acute (occurring within the first year) and late acute rejection episodes (occurring > 1 year from transplant), both major risk factors for chronic rejection (chronic allograft nephropathy), have

been found to be strongly associated with late graft loss (De Geest et al. 1995; Joseph et al. 2001; Sijpkens, Doxiadis, Mallat, Fijter, & Bruijn, 2003; Nevins & Thomas, 2009). In renal transplant recipients with ten years of graft function, allograft nephropathy (chronic rejection) was one of the identified causes of most graft loss (Matas, Gillingham, Humar, Kandaswaym, Sutherland, Payne, Dunn, & Najarian, 2008).

While the majority of prospective studies exploring IST nonadherence identified higher rates of acute rejection, graft loss, graft failure, and greater association with late acute rejection episodes in recipients identified as nonadherent (Morrissey et al., 2005; Nevins & Thomas, 2009; Brown et al. 2009; Nevins, Kruse, Skeans, & Thomas, 2001; Pinkey et al. 2009; Vlaminck et al. 2004; Hilbrands, Hoitsma, & Koene, 1995), two recent studies yielded conflicting results. A retrospective cohort study conducted by Denhaerynck and colleagues (2009) reported no association between nonadherence and graft failure / graft function in a sample of renal transplant recipients at least one year from transplant followed over a five year period. One study limitation identified by the researchers as contributing to these conflicting results was the exceptionally high rate of adherence (98.4%) that might have exceeded the threshold necessary to detect the effect of nonadherence. Other noteworthy research processes involved in the study included an adherence enhancing intervention carried out in nonadherent patients immediately following baseline measurement. In addition, the authors concluded that the use of newer, less nephrotoxic IST medications taken by 62% of the sample (mycophenolate mofetil, tacrolimus, sirolimus) may have reduced the detrimental effects of nonadherence on long-term renal function resulting in the inability to determine the mediating effects of nonadherence in the relationship (Denhaerynck et al. 2009). A more recent prospective cohort study of 243 deceased donor

recipients from 8 transplant centers conducted by Israni and colleagues (2011) followed participants 18 years of age and older who were recruited at the time of transplant and followed--up with telephone interviews after discharge and every six months for 36 months. Medication adherence was measured using electronic cap monitoring systems (eDEM© cap) during the initial 6 months posttransplant. While acute rejection occurred in 10% (n =25) of the sample, adherence was not associated with acute rejection or decline in glomerular filtration rate (Israni et al., 2011). Possibly contributing to the lack of association between adherence and outcomes in this study were two factors: 1) the limited time monitoring adherence potentially not representing adherence patterns during the remaining study period, and 2) electronic monitoring may have introduced measurement error by underestimating the amount of nonadherence (inability to prove ingestion) (Israni et al. 2011).

Studies exploring the economic outcomes associated with IST nonadherence are limited. Given that 36.4% of graft failures that occur within the first year following transplant result from IST nonadherence, $100 million in additional healthcare costs can be attributed to first year graft failures (Hansen, Seifeldin, & Noe, 2007). In addition, assuming 53% of rejection episodes were likely attributed to IST nonadherence, $13-$16 million dollars was necessary to treat and prevent graft loss (Hansen, Seifeldin, & Noe, 2007). More recent studies by Pinsky and colleagues (2009) and Evans and colleagues (2010) identified cost-related outcomes associated with nonadherence. Pinksy et al. (2009) in a survey of 254 U.S. renal transplant programs reported 68% of programs reported deaths and graft loss associated with cost-related IST medication nonadherence while Evans et al. (2010) in a retrospective study of 15, 525 first time renal

transplant recipients with Medicare coverage through the first year identified a $12,840.00 increase in individual three year healthcare costs in recipients with persistently low adherence.

Determinants of Nonadherence

Five categories of interrelated risk factors, reflective of the World Health Organization's (2003) categories, have been identified as influential to IST nonadherence in adult renal transplant recipients: 1) socioeconomic, 2) patient-related, 3) condition -related, 4) therapy - related, and 5) healthcare system / healthcare provider- related factors.

Socioeconomic-Related Variables

Socioeconomic factors, while relatively nonmodifiable in nature, have been the most widely studied factors within the adult renal transplant population. Consistent with global studies exploring predictive values of these factors (age, gender, race, income level, education) across illness categories (World Health Organization [WHO], 2003), results have been inconsistent within the adult renal transplant population. Similar to the multiple conceptual and operational definitions of adherence, multiple representations of socioeconomic variables within the adult renal transplant population (age, education, race, income level) may possibly contribute to the inconsistent findings.

The majority of studies conducted within the adult population consistently conclude younger age as being associated with nonadherence (Chisholm et al. 2005; Chisholm, Williamson, Goldfarb-Rumyantzev, Wright, Ragasa, Ostler, Van Orden, et al. 2011; Lance, & Mulloy, 2007; Denhaerynck et al. 2007; Frazier et al. 1994; Ghods et al. 2003; Greenstein & Siegal, 2000; Schweizer et al. 1990; Sketris et al. 1994). A review conducted by Denhaerynck et

al. (2005) suggested that studies failing to associate a younger age with nonadherence lacked a significant subsample of adolescents. The authors hypothesized that without a representative sample of adolescents, adherence might remain stable over the lifespan as long as cognition remained intact (Denhaerynck et al. 2005). Contrary to these studies, two recent studies reported findings that indicate nonadherence increases with age. In a study by Chisholm et al. (2008) results of the study found nonadherence increased as age increased. The second study identified 86% of the study population consisting of adults age 55 and older (mean sample age of 60.38 years) as being nonadherent with medications (Russell, Centingok, Hamburger, Owens, Thompson et al., 2010).

A few isolated studies have attempted to delineate age ranges of both younger and older recipients. Schwizer, Rovelli, Palmeri, Vossler, Hull, and Bartus (1990) differentiated between younger ($\leq$ 20 years) and older ($\geq$ 40 years) in age as reported in years, while Greenstein and Seigel (1998) reported older (mean age 47.9 years) and younger (mean age 41.1 years) recipients in terms of mean ages. Nevins, Kruse, Skeans, and Thomas (2001) defined "young" as < 21 years of age. A 1999 study comparing symptom frequency and distress in patients delineated 40 years of age as the median age separating older from younger patients (Teixeira De Barros & Cabrita, 1999). Chisholm-Burns and colleagues (2008) concluded that older recipients (those 60 years of age and older) were more likely to be nonadherent than younger recipients (those between age 18-60 years of age).

Variations exist in the operationalization of education with studies delineating low versus high levels of education; elementary, high school, and college; while others delineate education in the total number of years completed. Studies exploring the association of educational level

with adherence yielded similar conflicting results with no consistent association with IST nonadherence identified (Goldfarb-Rumyantzev et al. 2011; Butler et al. 2004; De Geest et al. 1995; Frazier et al. 1994; Ghods et al. 2003; Greenstein & Siegal, 1998; Raiz et al. 1999; Vasquez et al. 2003).

Studies exploring both race and income level have yielded mixed results making determination of a consistent relationship with IST adherence difficult (see Table 3). Multiple operational definitions of race evident in the current body of knowledge include: 1) whites, nonwhites; 2) black, 3) Caucasian, African American, Hispanic, and 4) black, nonblack. Socioeconomic status operationalized in terms of income level (mean annual income level), socioeconomic class (low, middle, high), and employment status (part-time, full-time, unemployed, student, retired; white collar, blue collar occupation) equally contribute to mixed results.

Patient-Related Variables

Of greater interest to clinicians are the modifiable patient-related or condition-related factors influencing the origins of IST adherence behavior. Health beliefs, conceptualized as the personal convictions that influence health behaviors (Moorhead, Johnson, Maas, & Swanson, 2008), encompass a combination of attitudes that include the perceived susceptibility of experiencing a harmful condition, the perceived seriousness of a condition, the perceived benefit the performance of the health behavior has in reducing the threat of the condition, and perceived barriers related to the negative aspects of a health behavior (Champion, 1984). A perceived need for medication (health beliefs) was found to contribute to IST nonadherence in several studies

(Butler et al., 2004; De Geest et al., 1995; Greenstein, & Siegal, 2000; Greenstein & Siegal, 1998; Raiz et al. 1999).

Qualitative studies support findings obtained through quantitative methods with regards to health beliefs. A phenomenological study by Orr et al. (2007) of 26 adult renal transplant recipients identified the theme of health beliefs as one of four patient perceived factors that influence IST medication adherence.

Research examining the effect of social interactions (social networks, social support) on IST adherence is limited. Social network variables such as living alone and/or being unmarried have been found to be associated with nonadherence (Butler et al. 2004; De Geest et al. 1995; Frazier et al. 1994; Raiz et al. 1999; Teixeira de Barros & Cabrita, 2000). Social support, defined as the existence or availability of a person or network of people that rely, care, and love an individual and on whom that same individual can rely (Sarason, Levine, Basham, & Sarason, 1983) is categorized as both perceived social support (individual's perception of available support) and received social support (support actually received by an individual) (Dobbels, Verleden, Vanhaecke, & DeGeest, 2006). Additional dimensions of social support identified in the literature include: 1) source of support, 2) satisfaction of support, and 3) type of support (emotional, instrumental or practical, informational, affirmational) (Chisholm-Burns, Spivey, & Wilks, 2010). The effect of social support on IST adherence among organ transplant recipients varies across studies. A meta-analysis by Dew et al. (2007) found poorer social support in solid organ transplants (kidney, heart, liver, pancreas, kidney/pancreas and heart and lung) to be associated with significantly greater IST nonadherence though the effect size was weak. While early multivariate models within the adult renal transplant population identified higher levels of

social functioning as associated with adherence, additional study results are inconsistent (Greenstein & Siegal, 2000). Kiley et al. (1993) identified nonadherence in renal transplant recipients to be associated with perceived amount of social support, while at the same time Frazier et al. (1994) found no relationship between social support and adherence. By contrast, a recent study conducted by Chisholm-Burns et al. (2010) identified a significant positive relationship between two types of social support (affectionate and instrumental support) and IST adherence.

Additional research into the contribution of the categories and dimensions of social support on long-term IST adherence is warranted due to the changing nature of both the scope of healthcare services and social support networks as time from transplant increases.

Condition-Related Variables

Symptom experience can be conceptualized as both symptom occurrence and symptom distress (Kugler, Geyer, Gottlieb, Simon, Haverich, & Dracup, 2009). Representing the cognitive component of symptom experience, symptom occurrence can be quantified by the frequency, severity, and duration of a given symptom, while symptom distress captures the emotional burden association with the symptom (Kugler et al. 2009). Though most often investigated within the context of its effect on quality of life, symptom experience (symptom occurrence / symptom distress), noted to be associated with an increased risk for nonadherence in early studies (Butler et al. 2004; Denhaerynck et al. 2007; De Geest et al. 1995; Greenstein & Seigel, 1998; Sketris et al. 1994; Teixeira de Barros & Cabrita, 1999). Symptom experience has only been explored recently in one isolated study conducted within the European population and

not within the context of adherence research but rather as a method of evaluating symptom profiles associated with immunosuppressant therapy (Koller, Denhaerynck, Moons, Steiger, Bock, & De Geest, 2010). In light of evolving immunosuppressant regimens, quantitative exploration of the effect of symptom experience on adherence is warranted.

Therapy-Related Variables

A variety of independent variables categorized as therapy-related variables have been explored in previous IST adherence studies. With the typical cost of IST therapy alone exceeding $10,000 annually, a few isolated studies have explored the effect of cost on IST adherence. Despite receiving medications free of charge, two studies concluded IST adherence to decrease over time suggesting drug cost alone as not influencing adherence (Chisholm et al. 2005; Chisholm et al. 2000).

Across the majority of studies, increased time from transplant, conceptualized as months, years, and mean years/months since initial transplant, has demonstrated association with nonadherence (Chisholm-Burns et al. 2008; Chisholm et al. 2005; Chisholm et al. 2000; Greenstein & Seigel, 2000; Greenstein & Seigel, 1998; Hardstaff, Green, & Talbot, 2003; Nevins, Kruse, Skeans, & Thomas, 2001; Nevins & Thomas, 2009; Sketris et al. 1994; Vasquez et al. 2003). Additional findings by Chisholm-Burns et al. (2008) identified a trend toward higher adherence rates in recipients four years or less posttransplant indicating a possible need for the implementation of interventions to support adherence as patients approach four to five years from transplant.

Across chronic illness categories, complex dose regimens have been found to contribute to poor medication adherence. In a systematic review of 76 studies encompassing a variety of disorders using electronic monitoring as the measure of adherence, researchers concluded mean dose-taking adherence declined as the number of daily doses increased (Claxton, Cramer, & Pierce, 2001). Adherence was significantly higher in once-daily dosing regimens versus three and four times daily regimens (Claxton et al., 2001).

Studies conducted within the transplant population have yielded similar results. In a study of 182 renal transplant recipients taking cyclosporine as a component of either dual or triple IST therapy, Sketric and colleagues (1994) noted the number of overall prescription medications significantly affected adherence. A later study, exploring adherence in a sample of 278 adult recipients recruited at the time of transplant and followed during the first year, identified a significant association between once daily versus twice daily dosing frequencies (Weng et al., 2005). Studies exploring the impact of medications prescribed to manage comorbid conditions in addition to IST medications noted similar results (Vasquez, et al. 2003; Goldfarb et al. 2009).

Efforts to improve IST medication adherence have led to the development of a reliable, prolonged formulation of tacrolimus (Advograft). Available since 2007, the more convenient once daily dosing regimen was preferred by 99.4% of a sample (n=1832) of European adult renal transplant recipients undergoing conversion from twice-daily to once-daily dosing with tacrolimus (Guirado, Cantarell, Franco, Huertas, Fructuoso, et al. 2011). Thirty-four percent of the same study population reported improved adherence, as measured by verbal self-report of

any deviations from dose schedule. Increased adherence was postulated to be due to increased convenience of not have an evening medication dose (Guirado et al. 2011).

Healthcare System-Related Variables

The influence of the healthcare system has been explored in two studies. Denhaerynck and colleagues (2006) compared IST adherence rates of American and European renal transplant recipients failing to identify specific healthcare system factors at the micro or macro level as significantly influencing nonadherence. An additional study conducted by Weng et al. (2005) identified transplant center characteristics as independently associated with adherence noting that the center may serve as a proxy for characteristics that promote adherence (cultural competency, staffing levels, frequency and quality of contact with providers, effectiveness of education). A recent study explored the effect of primary insurance on the risk of nonadherence (Chisholm et al. 2007). Researchers concluded that recipients with Medicare coverage were significantly less likely to be nonadherent to IST medications compared to those recipients who did not have Medicare coverage (Chisholm et al. 2007). A variety of private and government (Medicare, Medicaid) payor options are available to individuals undergoing renal transplantation with varying conditions of coverage. Medicare is the primary payor for approximately 70% of renal transplant recipients and a secondary payor for others (Woodward, Schnitzler, Lowell, Spitznagel, & Brennan, 2001). For patients eligible for Medicare coverage at the time of their transplant due to age, disability or entitlement secondary to end stage renal disease, Medicare pays 80% of costs associated with IST therapy (Cleemput, Kesteloot, Vanrenterghem, & De Geest, 2004). Duration of IST coverage varies under Medicare with individuals eligible solely

due to end stage renal disease entitlement losing coverage after 36 months. Though a study conducted by Yen and colleagues (2004) concluded extending Medicare Coverage of IST therapy for the life of a kidney transplant would result in both improved graft survival rates and significant cost savings to society, only a single isolated study has explored the association of payor type with nonadherence. With over 15,000 transplant recipients securing Medicare benefits by entitlement (U.S. Renal Data Systems, 2009), coupled with the increased interest in preemptive transplantation as a strategy to improve outcomes, the potential for an increase in the number of individuals with limited IST coverage warrants further exploration as a risk factor for nonadherence.

While research has identified several variables influential to IST adherence, to date, no study to date has focused on predictor variables that significantly influence IST adherence in a population of long-term (3 years or more from transplant) renal transplant recipients. Given the effect of nonadherence on graft outcomes and the influence of increased time since transplant on IST adherence, further exploration and identification of influencing factors in long-term adult renal transplant recipients is warranted if long-term outcomes are to improve.

Framework

Guiding the conduct of this study is the Health Decision Model, a third generation representation of the Health Belief Model proposed by Eraker, Kirscht, and Becker (1984). Within the context of adherence, the Health Belief Model (Becker, 1974) attributes the probability of adherence behavior to the interaction among an individual's perception of illness susceptibility and severity of a given health outcome with the benefits and barriers likely to be

encountered with a prescribed intervention. The Health Decision Model focuses on health decisions and the influence of patient preferences, health beliefs, and modifying factors on an individual's adoption of a health behavior (see Figure 1).

The ability of an individual to express preferences that influence health decisions has been associated with both decision analysis and behavioral decision theory (Eraker & Politser, 1982). Decision analysis provides a systematic process whereby individuals express preferences about risks and benefits associated with a therapeutic action. Behavioral decision theory extends decision analysis by identifying rules used by individuals to reduce complex decisions into simple ones (Eraker & Politser, 1982). Ultimately, the preferred course of action adopted by the individual reflects the outcome that offers the highest value.

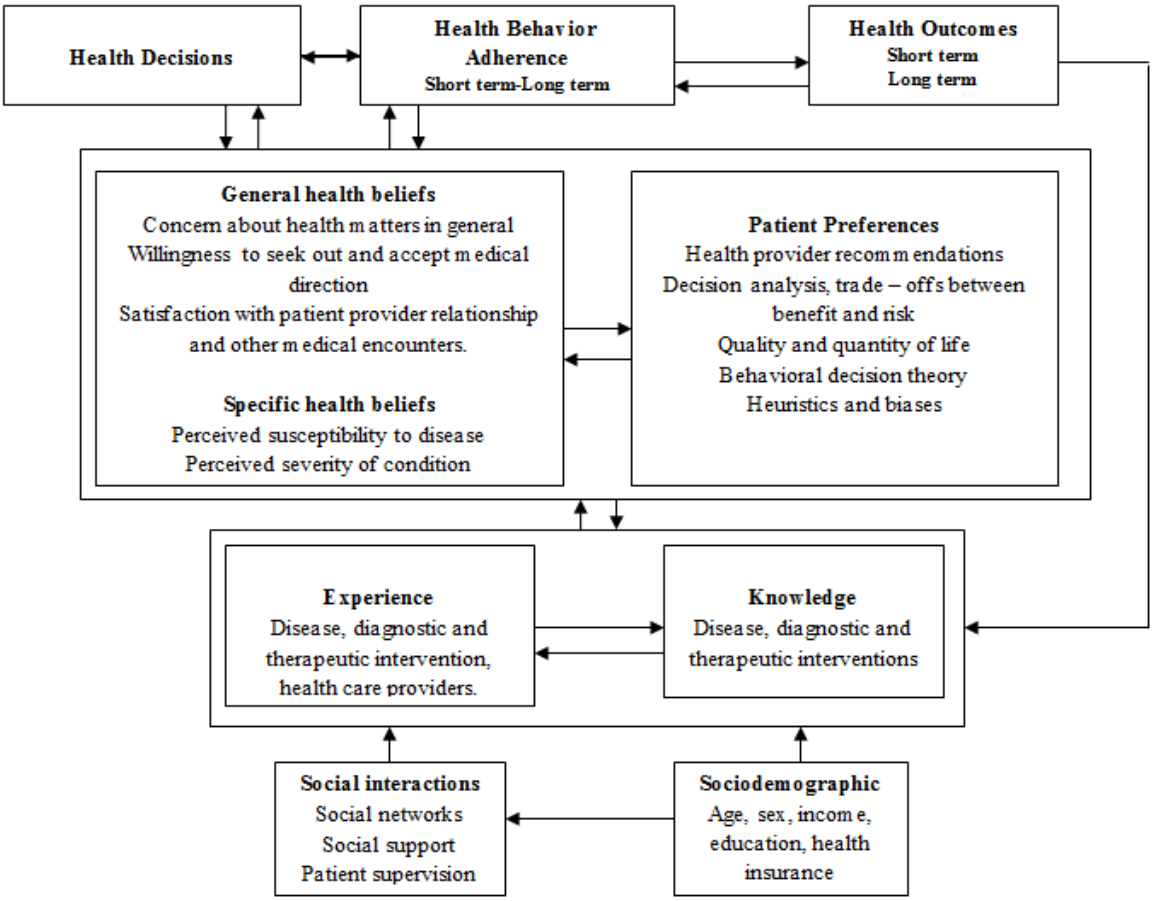
Health beliefs and several categories of modifying factors identified as components of the Health Decision Model are congruent with variables identified as contributing to adherence within the adult renal transplant population. Variables to be explored in this study, reflective of categories represented in the Health Decision Model include: 1) specific health beliefs regarding the necessity of prescribed medications as quantified by the Beliefs About Medicines Questionnaire, 2) symptom experience associated with the prescribed IST regimen as quantified by the Modified Transplant Symptom Distress/Symptom Occurrence scale, 3) social support as quantified by the Modified Social Support Survey, and 4) demographic variables categorized consistent with the Organ Transplant and Procurement Network national database (2012) as available. As illustrated by the bidirectional arrows and feedback loops depicted in the Health Decision Model, adherence behavior can also change health beliefs. In addition, while the degree of influence of many modifying factors may vary from individual to individual, this study

will seek to identify which combination of variables best predicts the probability of adherence behavior in the sample population.

Lacking in the current representation of health decisions and health behavior adherence (see Figure 1) are both the dimensions of medication taking adherence (taking, timing, omitting/ drug holiday, dose reduction) and the profiles of nonadherent individuals (accidental, invulnerable, decisive) identified in seminal work conducted by Greenstein and Siegal (1998). Representation of adherence dimensions will be captured through use of the self-report Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS) and examination of specific beliefs regarding IST medications using the Beliefs about Medicines questionnaire.

Three areas represented in the model will not be explored in this study. First, health outcomes associated with adherence behaviors including acute rejection, late acute rejection, and graft failure will not be explored within the context of this study as examination of these outcomes exceeds the proposed study purpose and design. Second, health decisions, or the process by which individuals make decisions that influence adherence will not be explored in this study. The decision to undergo transplantation as a treatment for end stage renal disease involves a decision making process that includes evaluating the lifelong therapy necessary to sustain the transplant. Given the long-term posttransplant sample population selected for study, key decisions related to adherence behaviors are assumed to have already occurred. Lastly, knowledge as it relates to IST interventions will not be explored. It was a study assumption that long-term participants would already possess the necessary knowledge regarding IST medications acquired through both pretransplant education and acute posttransplant care and follow-up.

Figure 1 depicts adaptations to the Health Decision Model reflective of this study. Figure 2 illustrates the adapted model that served as a guide for this study.



Adapted from "Understanding and Improving Patient Compliance" by Stephen A. Eraker and John P. Kirscht, 1984, *Annals of Internal Medicine, 100,* p.261

Figure 1 Health Decision Model

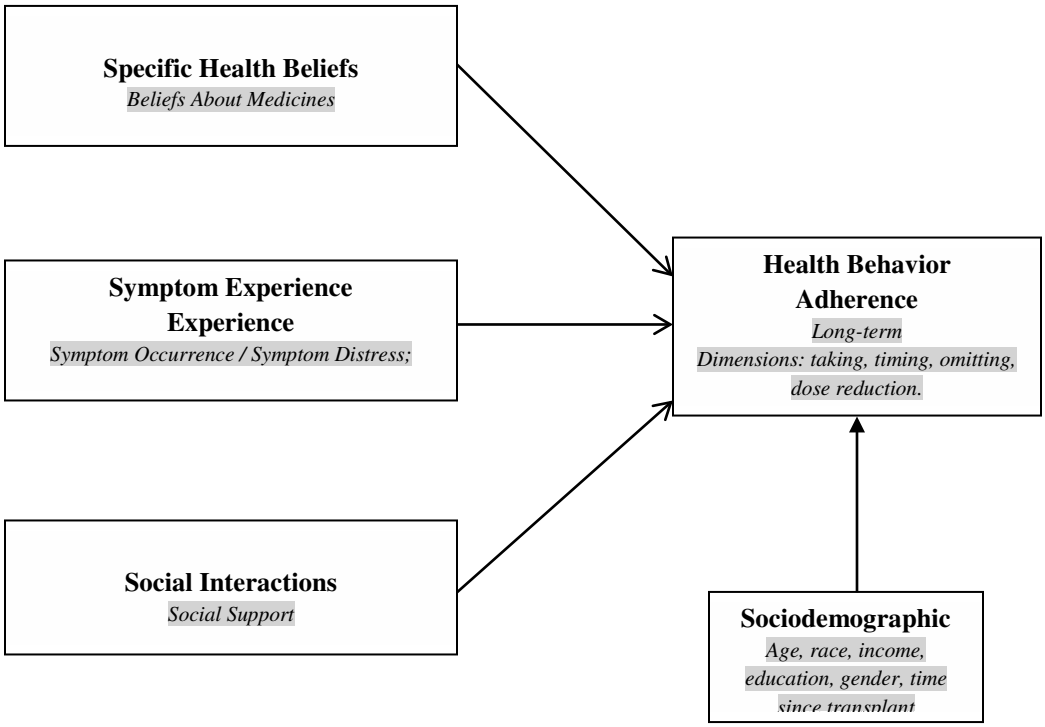


Figure 2: Adapted Health Decision Model

Summary

This chapter has presented the current state of the knowledge regarding immunosuppressant adherence in renal transplant recipients, issues with definition and measurement, and variables that impact optimum IST adherence. Strengths of the literature review are that much research has been conducted on IST adherence in renal transplant recipients since the early 1990's. Studies exploring the impact of nonadherence on acute and late acute rejection and graft loss have noted the influence on outcomes and propelled further research studies focused on identifying contributing factors. Additional studies exploring the impact of categories of influencing factors (socioeconomic, patient-related, condition-related, therapy related, and healthcare system / healthcare team-related factors) have led to predictive models and profiles that have identified variables amenable to intervention.

While strengths in the literature review were evident, weaknesses emerged. Given the focus on improving long-term outcomes, no study was identified that focused on exploring contributing factors in a population of long-term recipients. While many study populations included recipients that were several years from transplant, many studies included recipients as early as six months from transplant. In addition, immunosuppressive regimens have evolved over time potentially altering the symptom experience and complexity of dosing regimens. Finally, given the continued evidence surrounding the limitations of all methods of measuring medication adherence, only a few studies have explored the phenomenon using a combination of methods suggested to better represent the prevalence of adherence. This research study will add to the current state of knowledge by exploring factors known to influence IST adherence in a population of long-term renal transplant recipients helping to understand if the same factors

known to influence adherence in previous studies are the same or different in long-term recipients. Findings could identify modifiable factors amenable to interventions that could sustain or improve long-term IST adherence.

CHAPTER THREE: METHODS

The purpose of this study was to examine demographic variables, time since transplant, immunosuppressive agents, health beliefs, symptom experience, and social support and test their effect on IST adherence in a population of long-term adult renal transplants as predicted by the Health Decision Model (Eraker, Kirscht, & Becker, 1984).

Design

A cross-sectional, correlational design was used in this study to collect data at a single point in time using a voluntary convenience sample. This design was chosen to understand the relationships between the predictor variables of demographics, time since transplant, immunosuppressive agents, health beliefs, self-efficacy, symptom experience and social support and test their effect on the outcome variable of IST adherence in adult renal transplant recipients.

Sample

The study population consisted of a convenience sample of eligible adult renal transplant recipients who were three years or more from transplant and due to attend their annual transplant clinic appointment. The sample was obtained from patients receiving care at a large transplant center that met inclusion criteria and gave consent. Demographic data obtained at enrollment was used to validate meeting inclusion criteria.

Inclusion/Exclusion Criteria

To be included in the proposed study, sample participants must have been ≥ 21 years of age at the time of initial transplant; single kidney transplant recipient; able to speak, read, and understand the English language; had a functioning graft at the time of the study; and be three years or more from initial transplant. Graft function was determined by measured serum creatinine levels. A serum creatinine of 0.6-1.2 mg / dL from the clinic laboratory was considered normal range. Serum creatinine values obtained from outside laboratories were evaluated using reference values established by the transplant clinic laboratory. Transplant recipients with elevated serum creatinine levels were included in the study if the level was within the patient's maintenance baseline as determined by the transplant clinic provider.

Participants were excluded from the study if the elevated serum creatinine was not within the patient's maintenance baseline or if the participant had been retransplanted. Due to a lack of studies validating instruments in languages other than English, participants that did not speak, read or understand the English language were excluded from the study.

Determination of Sample Size

Power Analysis

An a priori power analysis was calculated by means of G*Power 3.0.8 (Faul, Erdfelder, Lang & Bucher, 2007) to determine the required sample size given a level of significance (α = .05), power of .80 (β = 0.20) and medium effect size (0.15) for linear multiple regression. Effect size was set as medium (Cohen, 1999) as the literature review was unable to provide a consistent estimate.

The primary research question contained six independent variables which were examined for relationships to the outcome variable of IST adherence. Statistical analyses planned included chi-square, Spearman correlation, independent-samples *t* test, and logistic regression. For logistic regression analysis with six predictor variables, anticipating a medium effect size (0.15), a sample of 98 was necessary. The sample size of 98 was further supported with recommendations for a ratio of subjects to independent variables of at least 15 :1 (Mertler & Vanatta, 2005; Tabachnick & Fidell, 2007), which was a minimum of 90 subjects.

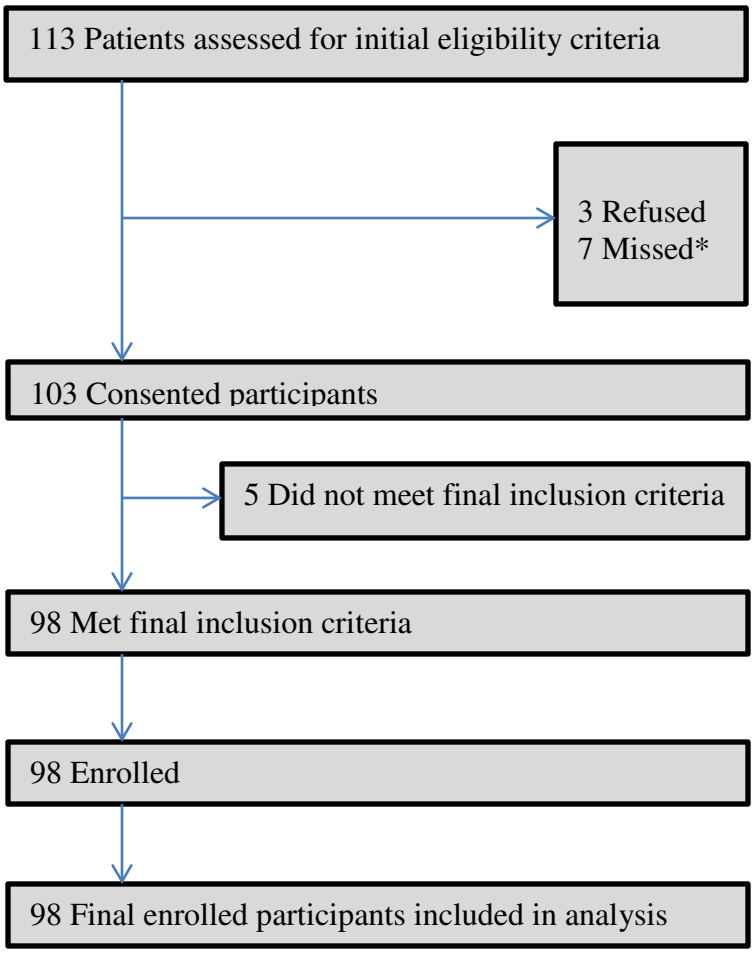
Setting

The site selected for the conduct of this study was Florida Hospital Transplant Clinic, a single site outpatient transplant clinic, in operation since 1973 and located in a large urban community in the Southeastern region of the United States. Since 1988, a total of 2,686 kidney transplants (living related-567; deceased donor-2119), procedures were performed across ethnic categories (White, Black, Hispanic, Asian, American Indian/Alaska Native, Pacific Islander, Multiracial) in the acute care facility associated with the outpatient clinic (Organ Procurement Transplant Network [OPTN], 2011). The site was selected due to the length of time in operation, the size of the recipient database, the scope of transplant services provided by the clinic, and the potential representation of the sample population.

Following completion of the acute care phase after renal transplantation provided by the Florida Hospital Transplant Clinic, primary care of the transplant recipient shifted to the local nephrologist for long-term care. Long-term follow-up care included monthly visits with the recipient's local nephrologist for the first year followed by every 2-3 months thereafter.

In addition to care provided by the local nephrologist, Florida Hospital Transplant Clinic followed the patient every 6 months during the first year posttransplant and annually thereafter. Immunosuppressive agents prescribed by providers at the clinic included tacrolimus (Prograf), sirolimus (Rapamune), cyclosporine (Neoral), mycophenolate mofetil (Cellcept), mycophenolate sodium (Myfortic), and prednisone. The primary IST regimen used included tacrolimus (Prograf) in combination with either mycophenolate mofetil (Cellcept) or mycophenolate sodium (Myfortic) with or without prednisone. If prednisone was a part of the IST regimen at 6 months posttransplant, doses were reduced monthly to a final dose of 5 mg/ day. Therapeutic monitoring of IST regimens included serum trough levels of tacrolimus (Prograf) and/or sirolimus (Rapamune) drawn within one week of the recipient's scheduled appointment if drawn at an outside lab or the day of the appointment if drawn at the Transplant Clinic lab. Therapeutic drug monitoring of mycophenolate mofetil (CellCept) and mycophenolate sodium (Myfortic) was not performed at this site. Dosage adjustments of Cellcept and/or Myfortic occurred only in the presence of adverse clinic effects (persistent, severe diarrhea, severe leukopenia < 2.0) and after consultation with clinic providers.

Approximately 30-45 patients were seen monthly for annual transplant follow-up evaluation. It was estimated that 10 patients per month would meet study inclusion criteria. The data collection period began July 2010 and concluded September 2011 with a total of 98 participants enrolled. Figure 3 provides an enrollment summary.



*Missed = cancelled appointment, no-show for scheduled appointment, or missed by PI

Figure 3: Enrollment Summary

Ethical Considerations

Protection of Human Subjects

Protection of study participants was accomplished by adhering to ethical and legal guidelines. All policies for protection of human subjects mandated by the institutional review boards of the University of Central Florida and Florida Hospital, and United States Federal Guidelines for conducting research with human subjects (U.S. Department of Health and Human Services (DHHS), 2001) were followed. Authorization to access individually identifiable health information was accomplished by having study participants sign a HIPAA Privacy Authorization form which was part of the informed consent process.

Informing Participants

The study was approved by the Institutional Review Boards of both Florida Hospital and the University of Central Florida (see Appendix H). Informed consent was obtained by the principal investigator.

Protecting Respondents

Individual responses to study instruments were anonymous; no identifying information, such as name or address was collected. Confidentiality was accomplished by assigning each participant a five digit study identification number which eliminated the discovery of any personal information. The created identification number was not linked to any personal medical record number or personal identifying data, and was used for all data. Only the researcher and

her research supervisor had access to the data files which were stored in a password protected computer.

Risks and Benefits to Participants

While there were no anticipated risks involved in participating it was possible that a participant could experience minor psychological discomfort when disclosing both symptom experiences as well as adherence behaviors. There were no direct benefits to participants aside from helping healthcare providers gain an understanding of factors that contribute to long-term IST adherence.

Data Collection

Sampling Procedure

Recruitment of participants was facilitated through use of the transplant center's recipient database. The transplant clinic coordinator in charge of scheduling annual follow-up appointments provided a weekly list of the number of potential participants meeting initial study inclusion criteria (age≥ 21, single transplant, and 3 or more years from initial transplant) to the principal investigator. The list provided to the principal investigator included only the date and time of the potential participant's annual clinic appointment. Initial interest in study participation was determined upon arrival of the potential participant for the annual visit and was facilitated by clinic staff. Recipients expressing an initial interest in study participation were approached by the principal investigator to obtain informed consent, and then screened for final study inclusion criteria (serum creatinine, English language skills). To enhance recruitment, a flyer

advertising the study was posted in the transplant clinic waiting room (see Appendix A). At month 12, initial study inclusion criteria was amended to exclude eligible participants previously enrolled in this study during the past year to avoid studying the same subjects twice.

Data Collection Process

Data collection was conducted by the principal investigator who was unknown to study participants and was not a member of the outpatient transplant clinic staff. Medical data (serum creatinine levels and serum drug assays) were obtained through a review of each participant's medical record conducted following the informed consent process. Medical data reviewed included serum creatinine and serum drug assay results as reported on the day of the participant's evaluation. The majority of participants had lab drawn in the clinic lab, a Clinical Laboratory Improvement Amendments (CLIA) certified lab. For participants with insurance designated requirements to use independent selected labs, only specimens drawn within the week prior to the annual clinic appointment were accepted.

All study instruments were administered by the principal investigator using an interview format in the private examination room located within the outpatient transplant clinic. The average wait time for clinic appointments was approximately 30-60 minutes for patients requiring laboratory services, and 15-30 minutes for patients not requiring laboratory services. Based on the identified time intervals, all potential participants underwent final screening and consenting immediately prior to their clinic appointment. If time permitted, all study instruments were administered prior the participant's medical visit. Participants were presented study instruments in the following sequence: 1) demographic survey, 2) the Beliefs About Medicines

Questionnaire (BMQ) (Horne, Weinman, & Hankins, 1999), 3) the Medical Outcomes Study (MOS) Modified Social Support Survey (MSSS) (Ritvo, Fischer, Miller, Andrews, Paty, & LaRocca, 1997), 4) the Basel Assessment of Adherence with Immunosuppressive Medication Scales (BAASIS) (De Geest, 2005), and 5) the Modified Transplant Symptom Occurrence and Symptom Distress Scale-59R (MTSOSD-59R) (Dobbels, Moons, Abraham, Larsen, Dupont, & De Geest, 2008). All instruments were administered in computer format using Survey Monkey™ (http://www.surveymonkey.com/). Use of the computerized methods for data collection were piloted with the first 5 subjects who found it acceptable. In addition to the instruments completed by study participants, a collateral assessment of adherence was completed by one transplant clinic registered nurse and the attending transplant clinic physician or nurse practitioner at the conclusion of the participant's examination.

In the event the participant declined use of the computer, or was unable to operate a computer, paper instruments were made available to the participant. Data obtained from paper instruments were entered into the Survey Monkey™ file by the principal investigator, with each survey item double checked for accuracy.

Approximately one hour was allotted during the participant's clinic appointment for instrument completion. All instruments completed on paper were examined for missing items prior to the participant leaving the study session. Participants were compensated with a $25.00 gift card at the end of data collection.

Data Collection Procedures

All study data recorded in the Survey Monkey™ program was downloaded by the principal investigator into a Microsoft Excel spreadsheet, and imported into the Statistical Package for the Social Sciences (SPSS) for Windows v 19.0 (SPSS, Inc., 2010) for statistical analysis. No errors in data entry were identified. Figure 4 summarizes study data collection processes and procedures.

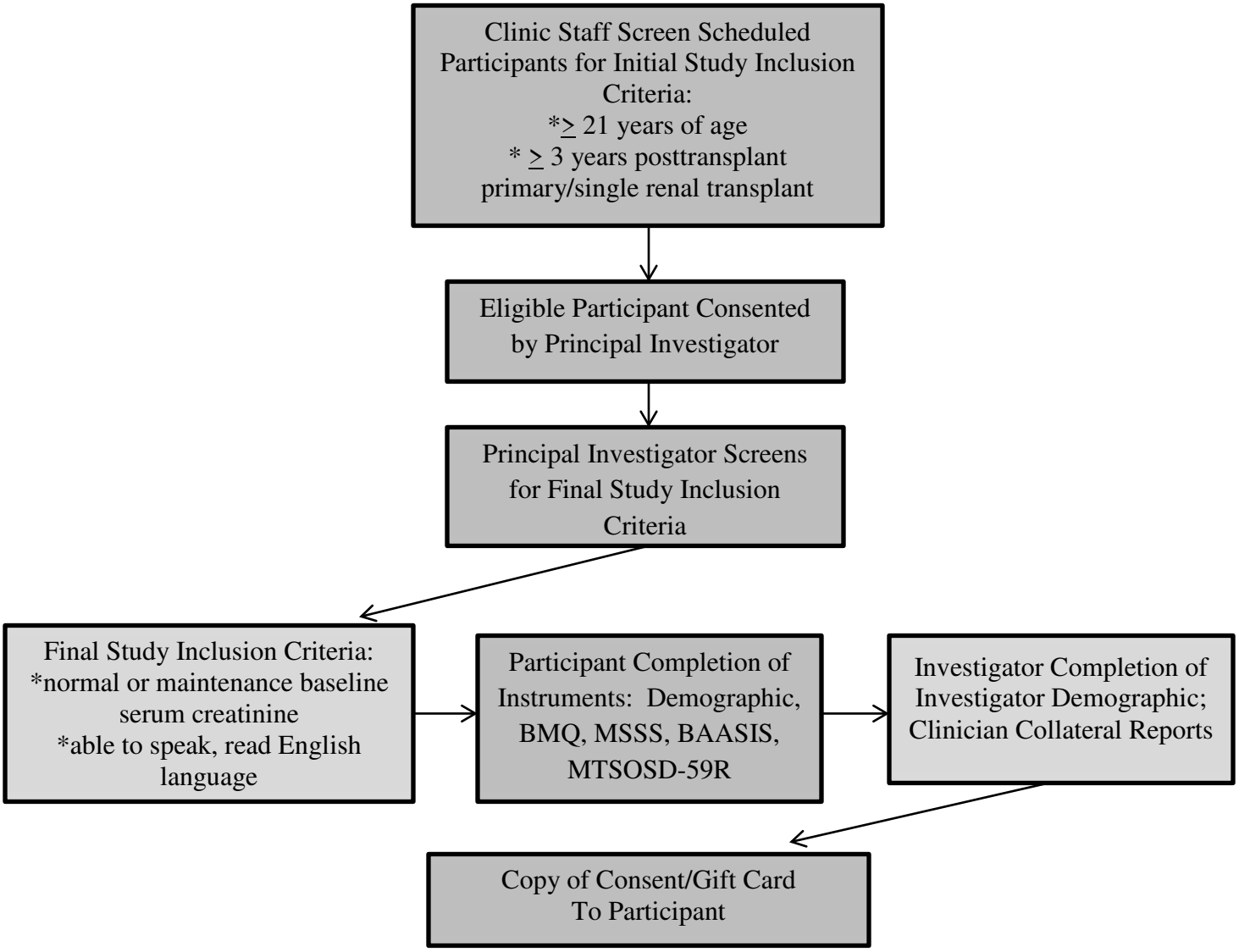


Figure 4: Data Collection Processes and Procedures

Data Storage

Access to study data was limited to the principal investigator and the chair of her dissertation committee. Once downloaded to the principal investigator's password protected computer, all data were backed up onto a compact disk (CD) and stored in a locked file cabinet in the principal investigator's office. At the end of a five year time frame, the CD and any other research materials will be destroyed.

Pilot Study

A pilot study was conducted on the first 5 participants for the following purposes: 1) testing the feasibility of study instruments, 2) determining clarity of instrument instructions, 3) obtaining an average estimation of instrument completion time, and 4) evaluating potential for interruptions in transplant clinic work flow. Data obtained from pilot study participants were included in the analysis as no instrument modifications were made. One minor modification was made to the study protocol allowing for administration of all study instruments prior to the participant's clinic appointment if time allowed.

Instrumentation

In addition to demographic information, participants completed the following data collection instruments: 1) Beliefs About Medicines Questionnaire (BMQ); 2) Medical Outcomes Study (MOS) Modified Social Support Scale (MSSS), 3) Basel Assessment of Adherence with Immunosuppressive Medication Scale (BAASIS), and 4) the Modified Transplant Symptom Occurrence and Symptom Distress Scale-59R (MTSOSD-59R) (see Appendix D). Each of

these measures demonstrated reliability and or validity either within the adult renal transplant or chronic illness populations. In addition, all measures had the same recall period of four weeks to reduce the potential for recall bias. Measures not evaluated previously evaluated within the adult renal population were tested for internal consistency reliability by means of Cronbach's alpha (α).

Demographic Survey

Demographic variables were collected using both participant and investigator collected instruments developed specifically for the study. All participant demographic variables were defined using categories as delineated by the Organ Procurement Transplant Network (2011) and/or the United States Census Bureau (2010).

Select demographic variables were calculated: age, time postttransplant, and the IST medication complexity index. Age at the time of study and time posttransplant were calculated and reported in years using birthdate, transplant date, and date of enrollment. Complexity of IST regimen was represented by a complexity index score calculated as the product of the number of IST medications in the regimen, the number of pills taken per day, and the number of times per day IST medications were taken.

Serum creatinine, as reported the day of enrollment, was obtained from the medical record. Serum creatinine values from all laboratory sources were evaluated using transplant clinic normal values (0.6-1.2 mg / dL) consistent with provider practice.

Serum drug assays were evaluated according to target therapeutic values determined by the transplant clinic for recipients beyond the sixth month from transplantation. These values

include: tacrolimus: 5-10 mg/L; sirolimus: 8-15 mg/L; and cyclosporine 150-250 mg/L. Therapeutic monitoring for mycophenolate mofetil (CellCept) and mycophenolate sodium (Myfortic) was not conducted at this facility.

Beliefs About Medicines Questionnaire

The Beliefs about Medicines Questionnaire (BMQ) constructed and tested by Horne, Weinman, and Hankins (1999) is composed of two sections: BMQ Specific and BMQ General. The BMQ Specific is further divided into two five-item subscales: *Specific Necessity* assessing a patient's beliefs about the necessity of prescribed medications, and the *Specific Concerns* assessing concerns about consequences of taking the same medications. The BMQ General section, which include the *General Harms* subscale and *General Overuse* subscale, assesses beliefs held by patients that often seek alternative methods of treatment such as herbal treatments or care from a homeopathic clinic (Horne et al., 1999). This section of the instrument was not applicable to the population under study and therefore was not used.

Validity

As part of instrument development, Horne et al (1999) established construct validity of instrument scales by performing exploratory principal component analysis. Scale items were derived from a pool of 34 items representing commonly held beliefs identified in the literature about medication. Data were based on a sample of 524 patients encompassing a variety of chronic illness categories (asthma n=78, diabetic n=99, renal n=47, psychiatric n=89, cardiac n=120, general medical n=91). Confirmatory factor analysis was conducted to verify the factor structure. Pearson correlation of items with predicted factor pattern yielded 0.88 for BMQ

Specific Necessity subscale and a 0.88 for the BMQ Specific Concerns subscale within the renal dialysis subsample.

Psychometric evaluation of the instrument provided evidence of both criterion-related and discriminant validity (Horne, Weinman, & Hankins, 1999). Criterion related validity was based on a two predictions: 1) that patients with stronger beliefs in the necessity of medication would be less likely to believe they can cope without medication (Specific Necessity subscale), and 2) that patients with strong concerns about prescribed medication who were more distrustful, would require more information about medication and would be more likely to change their current treatment regimen (Horne et al, 1999). Evidence for criterion-related validity was demonstrated with a negative correlation between scale scores and responses to the belief that they could cope without medicine (Specific Necessity, $p<.001$)) and a positive correlation between scale scores and the belief that they could not always trust medications (Specific Concerns, $p<.005$).

Discriminant validity was tested on the ability of the instrument to distinguish between different illness and treatment modalities. Testing hypothesized that beliefs about the necessity of medications would be influenced by the type of treatment for a specified illness (Specific Necessity) and Specific Concern scores would differentiate between different diagnostic groups with concerns varying based upon illness category. Predictions were confirmed by significantly higher Specific Concern scores for identified groups.

Reliability

Cronbach's alpha values for the renal dialysis diagnostic group established internal consistency of 0.55 for Specific Necessity and 0.73 for Specific Concerns. A study conducted

with the human immunodeficiency virus (HIV) population investigating beliefs associated with nonadherence to antiviral therapy identified internal reliability of both BMQ scales with Cronbach's alpha of 0.80 for Specific Necessity, and 0.82 for Specific Concerns (Horne, Buick, Fisher, Leake, Cooper, & Weinman, 2004).

While the BMQ has been used in a study conducted within the renal transplant population (Butler et al., 2004), no additional information specific to the validity and reliability of the instrument in the study was provided.

Scoring

Subscale items are measured using a five point Likert scale with one being "strongly disagree" and five "strongly agree." Possible scores for each subscale range from a minimum of five to a maximum of 25, with higher scores indicating stronger beliefs. A mean score for each subscale of the BMQ Specific was calculated by dividing the total scale score by the total number of items. The mean item score for each subscale was used to calculate a necessity-concerns differential (NCD) which was obtained by subtracting the Specific Concerns mean score from the Specific Necessity mean score providing a numerical indicator of the way an individual rates the need for medications to concerns over taking medications. A negative NCD value indicated an individual rated concern over taking medications higher than the beliefs about the necessity for taking medications.

Medical Outcomes Study Modified Social Support Scale

The Medical Outcomes Study (MOS) Modified Social Support Survey (MSSS) is a modified version of the Medical Outcomes Study Social Support Survey developed and tested by

Sherbourne and Stewart (1991). The 18 item MOS Modified Social Support Scale, one of ten subscales modified for use within the Multiple Sclerosis Quality of Life Inventory (MSQLI), measures perceived availability of various components of functional support (see Appendix K). Within the 18 items are four subscales representing multiple dimensions of social support. Four items (1,4,11,13) measure tangible support, eight items measure emotional/informational support (2,3,7,8,12,14,15,17), three items measure affectionate support (5,9,18), and three items measure positive social interaction (6,10,16). A five item version of the MOS MSSS is also available (MSSS-5) and consists of the 5 items (items 4, 6, 9, 11, and 17) that correlate most strongly with the total MSSS scale with all four subscales represented. The 18 item instrument was selected for use in this study due to the limited number of recent studies exploring social support within the renal transplant population.

Validity

Factorial validity, discriminant validity, and construct validity were established for the original Medical Outcomes (MOS) Study Social Support Survey by Sherbourne and Stewart (1991). Using responses from 2987 subjects, factor analysis discriminated four dimensions of social support: emotional / informational, tangible, affectionate, and positive social interaction. Confirmatory factor analysis of the original 19 items produced high correlations between emotional and informational support (0.99) while principal components factor analysis of the 19 original items show high loadings for all items ranging from 0.67-0.88. Discriminant validity was supported as single-item measures of structural support were distinct from functional support concepts. All items in the four subscales correlated higher with their own scale than with any other social support measure. All items exceeded convergent validity criteria with item

correlations ranging between 0.72-0.87 for tangible support, 0.80-0.86 for the affection scale, 0.82-0.90 for the emotional / information scale, and 0.87-0.88 for the positive interaction scale (Sherbourne & Stewart, 1991).

Confirmatory factory analysis of the original 18-item scale as well as two abbreviated versions was performed in a study of 330 mothers with a child in mental health treatment (Gjesfjeld, Greeno, & Kim, 2009). Both the twelve and four item scales demonstrates the best fit with reported Goodness of Fit Indices of .95 and1.00 respectively.

Reliability

Sherbourne and Stewart (1991) established internal-consistency reliability of scale scores using Cronbach's alpha. Pearson Product Moment correlations between support measures at enrollment and the same measures one year later estimated one year stability coefficients. Analysis performed for the Medical Outcomes Study sample found emotional/ informational support, tangible support, positive social interaction, and affectionate support correlations ranged between 0.91-.0.96. One year stability coefficients ranged between .72-.78 across all subscales (Sherbourne & Stewart, 1991).

The Consortium of Multiple Sclerosis Centers Health Services Research Committee in its construction of the Multiple Sclerosis Quality of Life Inventory (National Multiple Sclerosis Society, 1997), created the 18 item Modified Social Support Survey as one of 10 subscales used to measure health-related quality of life in multiple sclerosis patients. Analysis yielded Cronbach's alpha for tangible support, emotional support, affective support, and positive interaction support ranging between 0.87 and 0.85. The same Consortium reported a Cronbach's alpha of 0.88 for the abbreviated 5 item version of the MOS-MSSS scale.

To date, one study conducted within the adult renal transplant population (Chisholm-Burns, Spivey, & Wilks, 2009) has used the 5 item version of the MOS-MSSS scale; however validity and reliability statistics were not reported.

Scoring

Each of the 18 items are measured on a 5-point Likert scale (1= none of the time to 5= all of the time). The MSSS yields 4 subscale scores (Tangible Support [TAN], Emotional / Informational Support [EMI], Affectionate Support [AFF], and Positive Social Interaction [POS]. Raw scores range as follows for each subscale: 1) TAN 4-20; 2) EMI 8-40; 3) AFF 3-15; and 4) POS 3-15. Higher scale scores indicate greater perceived support.

Modified Transplant Symptom Occurrence and Symptom Distress Scale

The Modified Transplant Symptom Occurrence and Symptom Distress Scale (MTSOSD-59R), was developed as an updated and validated version of the 45 item Modified Transplant Symptom Occurrence and Symptom Distress Scale (Moons, De Geest, Versteven, Abraham, Vlamick, Moens, & Waer, 2001) to reflect the transplant patient's symptom experience with currently available immunosuppressive regimens (see Appendix K). The 59 item scale assesses symptom frequency and symptom distress associated with the use of current immunosuppressive agents (cyclosporine, corticosteroids, azathioprine, tacrolimus, mycophenolic-acid containing formulations, mTOR inhibitors and belatacept) (Dobbels et al., 2008).

Validity

To establish content validity, new items generated on the updated scale were added following a comprehensive review of the literature and analysis of adverse event forms of

belatacept studies, yielding a total of 76 items. A panel of 21 experts reviewed all items. Expert feedback resulted in the current 59-item version. Discriminant validity of the scale was tested in a pilot study of 24 adult renal transplant patients and 84 lung transplant patients (Dobbels et al., 2008). Discriminant validity was supported noting symptom profiles differed significantly with females demonstrating a higher symptom occurrence (p =0.096) and significantly higher symptom distress (p=0.017). In addition, patients with depressive symptoms had a significantly higher symptom occurrence (P=.030) and higher symptom distress (p=.006) compared to patients without depressive symptoms (Dobbels et al. 2008).

Reliability

An earlier study conducted for the purpose of establishing psychometric properties of the 29 item MTSOSD scale concluded that internal consistency assessment of the scale was neither useful or allowed (Moons, De Geest, Versteven, Abraham, Vlamick, Moens, & Waer, 2001). This finding was due to the presence of negative correlations in the correlation matrix which indicated symptoms were not correlated unidirectionally, violating a key assumption for the calculation of Cronbach's alpha. As such, internal consistency was not reported in this study.

To date, the MTSOSD-59R has been used in one study conducted within the adult renal transplant population exploring distress associated with adverse effects of IST medication (Koller et al. 2010). No additional information specific to the validity of the instrument in the study was provided.

Scoring

Symptom occurrence and symptom distress are scored on a 5- point Likert scale (0 = never occurring to 4 = always occurring; 0= not at all distressing to 4= terribly distressing).

Each item is a symptom scored in view of both symptom frequency of occurrence and symptom distress. In this study and consistent with previous research, ridit analysis, a statistical method used for analysis of ordinal level data (Delesis & Sermeus, 1996), was used to rank symptom occurrence and symptom distress items. Ridit scores range from a minimum of 0 to a maximum of 1. A ridit score of 0.5 represents equal probability, while ridit scores of > 0.5 represents higher probability. For the calculation of individual symptom distress ridits, symptoms reported as never occurring were coded as "missing data" and excluded from analysis to be truly representative of the symptoms they had. For final analysis, total individual participant symptom occurrence and symptom distress ridit scores were calculated as the sum of all individual item ridit values for each scale (symptom occurrence and symptom distress).

Basel Assessment of Adherence with Immunosuppressive Medication Scale

Developed by the Leuven-Basel Adherence Research Group (2005) to assess recent IST adherence (previous 4 weeks) in adult renal transplant recipients, the four item Basel Assessment of Adherence with Immunosuppressive Medication Scale (BAASIS) was conceptualized based on the dimensions of medication taking adherence (taking, timing, omitting / drug holidays, dose reduction). While there is a measure of IST adherence with demonstrated validity and reliability in the adult renal transplant population available (Immunosuppressant Therapy Adherence Scale [ITAS]), the BAASIS instrument was used for this study. Selection of this tool was based on more clearly defined scoring categories (0=never to 5=everyday BAASIS; 0%=none to > 50% = very frequent ITAS) as well as more recent recall of nonadherence (4 weeks-BAASIS; 3 months-ITAS) consistent with other instruments to be used in this study.

Validity

Early validation of the instrument has been reported in both the renal transplant population as well as the HIV population. In the adult renal transplant population, all four items of the BAASIS scale had superior sensitivity in detecting nonadherence compared with the Siegal Scale (Schäfer et al., work in progress of the Leuven-Basel Adherence Research Group). A study conducted within the HIV population demonstrated validity of the scale as a strong linear relationship was found between the number of missed doses and optimal viral suppression with the test for linear trend highly significant ($p < 0.0001$) (Glass, De Geest, Weber, Vernazza, Rickenbach et al., 2006).

Reliability

Internal consistency, as a measure of reliability of the BAASIS has not yet been established within the transplant population.

To date, the BAASIS instrument has been used in only one study conducted within the renal transplant population (Schmid-Mohler et al., 2010). No information specific to the validity and reliability of the instrument in the study was provided.

Scoring

Responses are scored on a 6 point Likert scale (0 = never to 5 = everyday). For the purpose of this study, nonadherence was defined as any self-reported nonadherence (response score 1 to 5) on any of the four items. Consistent with current research (Schmid-Mohler, 2009), *taking* adherence scores were dichotomized as "adherent" (0) and "nonadherent (1-5), and *timing* non-adherence scores were classified ordinally as "adherent" (0), "partial adherent" (1-2) and "nonadherent" (3-5).

Composite Score of Adherence

Current literature supports the use of a combination of adherence measures to increase the diagnostic accuracy of assessing adherence (Schäfer-Keller, Steiger, Bock, Denhaerynck, & De Geest, 2008).

Validity

Two composite adherence scores (CAS) were evaluated for validity. Composite adherence score 2 (CAS 2) which consists of a self- report of adherence, collateral reports of adherence, and nontherapeutic blood assay viability demonstrated the highest sensitivity (72.1%), followed by composite adherence score 1 (CAS1) (62.8%), validating both as acceptable screening measures for IST adherence (Schäfer-Keller et al., 2008). In the same study, validation of the different methods comprising the composite score identified the following: 1) non-therapeutic assay variability and self-reported nonadherence were found to correlate significantly ($p < .05$); 2) self-reported nonadherence correlated significantly with measures captured through electronic monitoring methods ($p < .05$); 3) clinician collateral reports significantly correlated with electronic monitoring dosing and taking adherence ($p < .05$); 4) CAS 1 correlated significantly with taking and timing adherence as well as non-therapeutic blood assay variability (ranging from $r_{rho} = 0.129$ [$p<.05$] to $r_{rho} = 0.333$ [$p<.05$]); and 5) CAS 2 (patient self-reported adherence, clinician collateral report of adherence, and nontherapeutic blood assay variability) correlated significantly with electronic monitoring drug holidays , dosing, taking, and timing adherence (ranging from $r_{rho} = 0.135$ [$p<.05$] to $r_{rho} = 0.289$ [$p<.05$]) (Schäfer-Keller et al., 2008).

Composite Score of Adherence Components

BAASIS

For use as the self-report component of the final CAS score, a total BAASIS score was calculated as the sum of response scores to the four scale items. Any self-reported nonadherence on any of the instruments four items classified the participant as nonadherent. For final analysis as a component of the CAS score, the total BAASIS score was dichotomized (adherent, nonadherent), reverse scored, and coded in SPSS as "0"= nonadherent and "1" = adherent.

Collateral Report of Adherence

Collaterally reported adherence, defined as a method of providing information about a patient's medication taking behavior as reported by a third party (De Geest, Abraham, & Dunbar-Jacob, 1996), was measured using two reports: one provided by the transplant clinic registered nurse, and one by the attending transplant clinic provider (physician or nurse practitioner) (see Appendix K). Clinicians were asked to rate the participant's overall general immunosuppressant adherence as "good" (0), "fair" (1), or "poor (2)". Consistent with previous research (Schmid-Mohler et al., 2009), clinician collateral responses were combined and scored as "adherent" (both clinician's estimated "good"), "partially adherent" (one clinician estimated "fair" or "poor"), and "nonadherent" (both clinicians estimated "poor"). Total combined scores ranged from 0-4 (0 = "adherent", 1-3 "partially adherent", 4 = "nonadherent"). For final analysis as a component of the composite adherence score (CAS) total collateral report of adherence scores were dichotomized (adherent / nonadherent), and coded in SPSS as "0"= nonadherent, and "1" = adherent.

Nontherapeutic Blood Assay

Serum drug assay was assessed using a single serum trough level for the monitored IST agent. A therapeutic drug range was specified for each immunosuppressive agent based on clinical guidelines used at the selected study site. Therapeutic ranges were defined as follows: tacrolimus (Prograf), 5-10 ng / mL; sirolimus (Rapamune), 8-15 ng / mL; and cyclosporine (Sandimmune), 15-250 ng /mL. Mycophenolate mofetil (Cellcept) and mycophenolate sodium (Myfortic) therapeutic assays were not currently monitored at the study site. Serum drug assays were scored as "adherent" (0) if assessed value was within therapeutic range, and "nonadherent" (1) if outside normal range. For final analysis as a component of the composite adherence score (CAS) serum drug assays scores were dichotomized (adherent / nonadherent), and coded in SPSS as "0"= nonadherent, and "1" = adherent.

CAS Scoring

For final analysis, the composite adherence score (CAS) was calculated and consisted of a self-report measure of adherence (BAASIS), two clinician collateral reports of adherence, and a single serum IST medication trough level. Consistent with the literature, cut-off criteria for nonadherence consisted of self-reported nonadherence, and / or at least 1 clinician's response of "fair" or lower adherence, and / or non-therapeutic drug assay (Schäfer-Keller et al., 2008). The sum of the dichotomized scores for the BAASIS, clinician collateral reports, and serum drug trough level were totaled. Final CAS cut score was coded in SPSS as "0"= nonadherent, and "1" = adherent.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS; version 19.0). All data were prescreened prior to analysis by exploring descriptive statistics, characteristics of distribution (central tendency, variability, skewness, kurtosis), and for the presence of missing values and outliers. Depending upon the level of measurement and distribution of each variable, data were expressed in frequencies or means and standard deviations. Spearman correlation coefficients were calculated to determine the strength of the relationship between independent predictor variables and the dependent outcome variable of adherence. Independent-samples *t* tests were used for two group comparisons of continuous variables. A significance level of $\leq .05$ was considered statistically significant.

To answer the primary research question, logistic regression was performed. For logistic regression, the model fit, classification table, and summary of model variables were evaluated to determine the accuracy of the developed regression model.

Statistical Assumptions

Descriptive statistics were computed for all variables. Data were explored to evaluate normality of distribution and homogeneity of variance. Distributions were evaluated by means of histograms, skewness and kurtosis, and the Kolmogorov-Smirnov *(D)* statistic. Data from different participants were independent and not influenced by the behavior of other participants. Nonparametric tests were performed for those variables not meeting assumptions of normality and for determining the strength of the relationship between variables measured at the ordinal level. Parametric tests identified as robust and tolerant of violations of assumption of normality

were performed to compare means across groups. Homogeneity of variance was assessed using Levene's test (Mertler & Vanatta, 2005).

Prior to logistic regression analysis, data were prescreened for outliers, and predictor variables were evaluated for multicollinearity. Goodness-of-fit test was performed to assess the fit of the model to the data.

Quality Control

All data were prescreened and evaluated for missing values and outliers. Missing values were minimal and were replaced with the mean or mode of the population depending upon the level of variable measure. Outliers were identified by inspection of box plots. Outliers were included in analysis using nonparametric tests as these tests are less sensitive to the effects of outliers. Outliers were included in analysis using robust parametric tests that are tolerant of violations of normality produced by the effects of outliers.

Hypothesis Testing

Univariate analysis was performed to assess the relationship between all demographic variables, BMQ, MSSS, and MTSOSD-59R ridit scores and the outcome variable of adherence. All independent variables demonstrating a significant relationship to the dependent variable were entered into the final logistic regression analysis.

In addition to the primary research question, ten hypotheses were tested. Hypothesis 1, 2, 3, 5, 7, and 9 examined the relationship between one predictor variable and the outcome variable of composite adherence group classification. Given the ordinal level of measure of the dependent variable, these hypotheses were tested using Spearman's correlation coefficient.

Hypothesis 4, 6, 8, and 10 explored differences in variable scale scores between composite adherence group classifications. Analysis was performed using independent-samples *t* test due its robust nature in tolerating violations of the assumption of normality. Independent-samples *t* tests were also used in to assess differences in scores of variable scales between age, gender, and time posttransplant groups.

Spearman Correlation Coefficient

Spearman correlation coefficient examines the strength of the relationship between two variables.

H 1: There will be a significant negative relationship between the predictor variable of time posttransplant as measured in years and composite adherence score classification.

H 2: There will be a significant relationship between the predictor variable of age as as measured in years and composite adherence classification.

H 3: There will be a significant relationship between medication complexity index scores and composite adherence group classifications.

H 5: There will be a significant relationship between the predictor variable of health beliefs as measured by BMQ Necessity and BMQ Concerns scores and composite adherence group classification.

H 7: There will be a significant positive relationship between the predictor variable of social support as measured by MSSS subscale and total scale scores and composite adherence group classification.

H 9: There will be a significant negative relationship between the predictor variable of symptom experience as measured by MTSOSD-59R total ridit scores and composite adherence group classification.

Independent-Samples *t* Test

Independent-samples *t* test compares the means of two samples. While scores should be normally distributed, the test is robust and can handle violations of the assumption of normality.

H 4: There will be a significant difference in IST complexity index scores between composite adherence group classifications.

H 6: There will be a significant difference in BMQ Necessity subscale, BMQ Concerns subscale, and BMQ Necessity / Concerns differential scores between composite adherence group classifications.

H 8: There will be a significant difference in MSSS subscale and total scale scores between composite adherence group classifications.

H 10: There will be a significant difference in MTSOSD-59R total ridit scores between composite adherence group classifications.

Logistic Regression

Logistic regression seeks to identify which combination of independent variables best predicts membership into groups.

Primary research question: which of six predictor variables-demographic variables, time since transplant, immunosuppressive agents, health beliefs, social support, and symptom experience-are most influential in predicting IST adherence in long-term adult renal transplant recipients?

Methodological Limitations

Methodological limitations identified in the current study are related to issues with design, sampling, measurement, and statistical analysis.

Design

Use of a cross sectional, correlational design isolates exploration of the continuum of nonadherence to one point in time. Many researchers in the field hold the belief that nonadherence is not an isolated phenomena but rather a dynamic phenomenon that exists on a continuum, changing over time, with all patients most likely demonstrating nonadherence behavior at any given time. Within the context of this study, the design limits the assessment of nonadherence to one point in time.

Sampling

Use of a convenience sampling plan is not without limitations. Consistent with nonprobability methods, there is potential for systematic over or under-representation of population elements. As a result, the sample obtained for this study may not be representative of the target population limiting generalizability of findings. Additional potential for bias exists due to the likelihood that adherent participants presenting for annual follow-up are more likely to adhere to all aspects of a treatment plan including appointments.

Measurement

While a combination of methods was used to measure adherence, each is not without limitations. Self-report measures of adherence run the risk of underreporting nonadherence while serum drug assays of drugs with short half-lives provide limited understanding beyond recent adherence patterns. A single, isolated serum drug assay was used as the component of composite adherence score, rather than assessing variability over several trough blood level results. In addition, clinician collateral reports used in this study were provided by two clinic providers, both of whom had limited first-hand knowledge of the patient's adherence behaviors in the year prior to the clinic visit.

Statistical Analysis

For the purpose of this study, nonadherence was a dichotomized variable (all or nothing phenomena). While necessary to reduce response bias associated with self-reported measures of adherence, dichotomizing the phenomena can result in loss of dimensionality. Finally, analysis of data using logistic regression requires caution when interpreting results as findings do not indicate causality but rather demonstrate association and prediction (Polit & Beck, 2008).

Summary

This research study attempted to examine the impact of six predictor variables-demographic, time posttransplant, immunosuppressant regimen, health beliefs, social support, and symptom experience on IST adherence. This chapter presented a description of study

procedures, a description of study participants, and explanations for the choice of statistical tests used for hypothesis testing.

CHAPTER FOUR: RESULTS

The purpose of this study was to examine demographic variables, time since transplant, immunosuppressive agents, health beliefs, social support, and symptom experience and test their relationship to adherence based upon the Health Decision Model (Eraker, Becker, Strecher, & Kirscht, 1984).

The purpose was achieved through the testing of ten hypotheses. In these hypotheses, demographic variables, time since transplant, IST agents, health beliefs, social support, and symptom experience were considered independent variables while immunosuppressant adherence was considered the dependent variable.

Data were collected over a fourteen month period. Combining both participant and investigator completed instruments resulted in a total of 91 scale items and 18 demographic items. Data were analyzed using SPSS 19.0 for Windows.

Description of the Sample

Of the 106 individuals approached, a total of 103 (97%) consented to participate. Of these, 98 (95%) met final study inclusion criteria and were used in the data analyses. The sample (N = 98) was represented by males (n = 57, 58%) and females (n = 41, 42%) ranging in age from 25 to 84 years (M = 57.2, SD = 12.75) with 43% (n = 42) of the sample < 55 years of age and 54.1% (n = 53) of the sample ≥ 55 years of age. Time posttransplant ranged from 3 years to 14 years (M=4.9, SD = 1.72) with 67.3% (n =66) of the sample 3-≤ 5 years posttransplant, and 32.7% (n = 32) of the sample 6 years or more from transplant. The typical participant was a 57.19- year old nonhispanic, white married male, 4.95-years from transplant, not currently

employed, receiving an annual income ranging between $10,000-$29,999 per year, having some college education, and insured by Medicare. In addition, the typical participant's IST regimen included 2.44 medications and consisted of tacrolimus (Prograf) in combination with either mycophenolate sodium (Myfortic) or mycophenolate mofetil (Cellcept) with or without Prednisone. Additional demographic information for the sample is presented in Table 2.

Table 2 Demographic Characteristics of the Sample

Variable	*n*	*Frequency %*	*Mean*	*SD*	*Range*
Age	98		57.19	12.74	25-84
Age					
< 55 years of age	42	42.9			
≥ 55 years of age	53	54.1			
Gender					
Male	57	58.2			
Female	41	41.8			
Time Posttransplant	98		4.95	1.71	3-14
Time Posttransplant					
3-5 years	66	67.3			
6 years or greater	32	32.7			
Race					
White	69	70.4			
African American	27	27.6			
Asian	2	2			
American Indian / Alaska Native	0	0			
Native Hawaiian / Pacific Islander	0	0			
Ethnicity					
Not Hispanic or Latino	80	81.6			
Hispanic or Latino	18	18.4			
Marital Status					
Married / Living Together	69	70.4			
Single	12	12.2			
Separated / Divorced	10	10.2			
Widowed	7	7.1			

Variable	*n*	*Frequency %*	*Mean*	*SD*	*Range*
Employment Status					
Not Currently Employed	62	63.3			
Full-time (36-40 hours per week)	31	31.6			
Part-time (< 36 hours per week)	5	5.1			
Highest Level of Education					
Some College	31	31.6			
High School or Equivalent	29	29.6			
Bachelor's Degree	21	21.4			
Vocational / Technical School (2 year)	11	11.2			
Master's Degree	6	6.1			
Annual Reported Income					
<$10,000	12	12.2			
$10,000-$29,999	32	32.7			
$30,000-$59,999	26	26.5			
$60,000-$99,999	17	17.3			
$100,000-$249,999	10	10.2			
Primary Insurance					
Medicare	54	55.1			
Private Insurance	39	39.8			
Medicaid	3	3.1			
Self-Pay	2	2			

Variable	*n*	*Frequency %*	*Mean*	*SD*	*Range*
Immunosuppressant Medication					
tacrolimus (Prograf)	92	93.9			
prednisone	53	54.1			
mycophenolate sodium (Myfortic)	43	43.9			
mycophenolate mofetil (CellCept)	40	40.8			
sirolimus (Rapamune)	6	6.1			
azathioprine (Imuran)	3	3.1			
lefluonamide (Arava)	2	2.0			
Number of IST Medications in Regimen	98	-	2.44	.593	1-4
Total IST Pills in Medication Regimen	98	-	4.73	1.36	2-8
Total Times Per Day Taking Meds	98	-	1.99	.176	1-3
IST Medication Complexity Index	98	-	24.31	11.56	4-72
Serum Creatinine	98	-	1.34	.509	0.62-4.29
Serum Drug Assay					
tacrolimus (Prograf)	94	-	6.93	2.73	1.50-18.30
sirolimus (Rapamune)	5	-	11.26	4.56	6.2-18.7

Adherence Demographics of Sample

A composite adherence score (CAS) (self-report nonadherence, one clinician response of "fair" or lower adherence, and non-therapeutic serum drug assay) determined adherence classification of study participants. Of the total sample population ($N = 98$), 39.8% ($n = 39$) were classified as adherent, with 60.2% ($n = 59$) identified as nonadherent. Of the participants identified as adherent ($n = 39$, 39.8%), 59% ($n = 23$) were males and 41% ($n = 16$) were females. Adherent participants were typically less than 55 years of age ($n = 23$, 59%) and 5 years or less from time of initial transplant ($n = 27$, 69.2%). Eighty-three percent ($n = 81$) of participants were adherent to medication taking behaviors while 64.3% ($n = 63$) were adherent to medication timing behavior. Table 3 summarizes adherence demographics of the sample.

Table 3 Adherence Demographics of Sample

Composite Adherence Score (CAS) Component	Nonadherent		Adherent	
	n	*Frequency %*	*n*	*Frequency %*
BAASIS	41	41.8	57	58.2
Clinician Collateral	5	5.1	93	94.9
Serum Drug Assay	31	31.6	67	68.4
Composite Adherence Score	59	60.2	39	39.8

Scores on Adherence Measures

Prior to hypotheses testing, descriptive statistics were obtained to describe and summarize data for adherence measures. Continuous independent variable scores were examined for measures of central tendency, outliers, and characteristics of distribution.

Measures of Central Tendency

Measures of central tendency for continuous independent variables were calculated. Overall, study participants demonstrated strong beliefs regarding the necessity for taking medications. The mean Necessity Concerns Differential score (m = 2.42) indicated study participants rated the beliefs about the necessity for taking medications higher than the concerns over taking medicines as further supported by the overall low mean BMQ Concerns subscale score. Of the dimensions of social support, participants perceived greater overall emotional / informational social support (m = 33.78). Participants also experienced a higher degree of symptom frequency as compared to symptom distress. Table 4 summarizes measures of central tendency for continuous independent variables used in this study.

Table 4 Measures of Central Tendency for Independent Variables

Independent Variable	*N*	M	SD	Range
Age	98	57.17	12.75	25-84
Time posttransplant	98	4.95	1.72	3-14
IST Medication Complexity Index	98	24.31	11.56	4-72
Beliefs About Medicines (BMQ)				
Necessity subscale	98	23.01	3.61	5-25
Concerns subscale	98	10.93	3.78	5-23
Necessity Concerns Differential	98	2.42	1.14	-1.60-4.0
MSSS	98			
Tangible (TAN)	98	16.72	4.20	4-20
Positive Social Interaction (POS)	98	13.12	2.46	5-15
Emotional / Informational (EMI)	98	33.78	7.04	8-40
Affectionate (AFF)	98	13.69	2.15	4-15
MSSS Total	98	19.33	3.51	7-23
MTSOSD-59R Total Ridit Scores	98			
Symptom Distress	98	9.81	6.10	0-30.4
Symptom Frequency	98	29.81	6.02	19.1-43.5

Outliers

Histograms and boxplots were visually inspected to identify outlying cases. Minimal outliers were identified for time posttransplant (2), IST medication complexity index (1), and MTSOSD-59R symptom distress total ridit scores (1) with no outliers noted to be severe, extending 3 box lengths beyond the plot. All MSSS scales had identifiable outliers (TAN =6; POS =3; EMI =7; AFF =4; MSSS total =7); however, no outliers extended beyond three box lengths. Both BMQ subscales contained minimal outliers (BMQ Necessity =3; BMQ Concerns =1) with both including extreme outliers extending beyond 3 box lengths from the plot (BMQ Necessity =2; BMQ Concerns =1).

All outlying cases were considered to be both minimal in frequency and valid components of the sample and were included in the analysis.

Tests of Normality of Distribution

Normality of distribution of all continuous independent variable values / scores (age, time posttransplant, IST medication complexity index, BMQ subscales, MSSS subscales, MSSS total scale, MTSOSD-59R symptom frequency total ridit, MTSOSD-59R symptom distress total ridit) was calculated using measures of skewness, kurtosis, and calculated Kolmogorov-Smirnov (K-S) value. Results showed values for age and scores for the BMQ Concerns, and MTSOSD-59R Symptom Frequency total ridit scores were normally distributed within adherence classifications as evidenced by both skewness and kurtosis values between -1 and 1 and further supported by non-significant K-S values. Table 5 summarizes results.

Table 5 Tests of Normality of Distribution

Variable	Skewness		Kurtosis		Kolmogorov-Smirnov (K-S)		*p*	
	Nonadherent	Adherent	Nonadherent	Adherent	Nonadherent	Adherent	Nonadherent	Adherent
Age	-.373	-.107	-.423	-.542	.094	.102	.200	.200
Time posttransplant	1.197	.360	6.520	-.890	.145	.136	.003	.068
IST Medication Complexity Index	1.086	3.291	.244	-.954	.188	.221	.000	.000
Beliefs About Medicines (BMQ)								
Necessity	.311	.378	.613	.741	.290	.258	.000	.000
Concerns	.551	.612	-.029	.489	.114	.140	.053	.051
Necessity Concerns Differential	-.968	-.761	.753	.709	.113	.144	.060	.041
MSSS								
Tangible (TAN)	-1.165	-2.009	.476	3.742	.187	.271	.000	.000
Positive Social Interaction (POS)	-1.160	-1.709	.734	2.417	.226	.332	.000	.000
Emotional / Informational (EMI)	-1.182	-1.603	1.172	1.706	.173	.238	.000	.000
Affectionate (AFF)	-2.216	-1.916	5.412	4.110	.306	.329	.000	.000
MSSS Total	-1.258	-1.660	1.527	2.092	.150	.234	.000	.000
MTSOSD-59R Total Ridit Scores								
Symptom Frequency	.309	.444	-.955	-.268	.105	.114	.166	.200
Symptom Distress	.466	.981	-.459	1.800	.103	.140	.193	.051

Estimation of Internal Consistency

Given that the target sample size was achieved, reliability of each of the variable scales was estimated by means of Cronbach's alpha (*a*). The BMQ necessity subscale achieved an acceptable alpha value greater than .70: BMQ necessity subscale ($n = 98$, $\alpha = .92$). The BMQ concerns subscale ($n = 98$, $\alpha = .68$) fell just short of an acceptable estimate. These alphas compared favorably to those reported by earlier researchers: BMQ necessity subscale ($\alpha = .55$) and BMQ concerns subscale ($\alpha = .73$) (Horne et al., 1999).

All subscales of the MSSS social support scale as well as the total MSSS scale score achieved equally acceptable alpha values: four item TAN ($n = 98$, $\alpha = .93$), eight item EMI ($n = 98$, $\alpha = .95$), three item AFF ($n = 98$, $\alpha = .88$), three item POS ($n = 98$, $\alpha = .93$), and eighteen item MSSS total score ($n = 98$, $\alpha = .96$). Values compared favorably to previously published values: TAN ($n = 98$, $\alpha = .84$), EMI ($n = 98$, $\alpha = .80$), AFF ($n = 98$, $\alpha = .86$), POS ($n = 98$, $\alpha = .87$), and MSSS total score ($n = 98$, $\alpha = .88$) (National Multiple Sclerosis Society, 1997). Table 6 summarizes internal consistency estimation values.

Consistent with previous research reporting psychometric properties of the MTSOSD-59R scale, internal consistency was not appropriate or permitted and thus not estimated for the purpose of this study.

Table 6 Estimation of Internal Consistency as Reliability

Instrument	*N* of items	Chronbach's alpha
Beliefs About Medicines (BMQ)		
Necessity	5	.92
Concerns	5	.68
Modified Social Support Scale (MSSS)		
Tangible (TAN)	4	.93
Emotional / Informational (EMI)	8	.95
Affectionate (AFF)	3	.88
Positive Social Interaction (POS)	3	.93
MSSS Total Score	18	.96

Hypothesis Testing

Ten hypotheses were posed based on the Health Decision Model as adapted for use in this study (see Figure 1). Due to the dichotomous nature of the dependent variable, the relationship between independent variables and composite adherence group classifications (hypotheses 1, 3, 5, 7, and 9) were tested using Spearman's correlation coefficient. The robust independent samples *t* tests was used to test for differences in mean independent variable scores among adherence classification groups and specified demographic groups (age, gender, time posttransplant). Independent variables that demonstrated a significant relationship to adherence group classification were entered into the final regression analysis.

Categorical Demographic Variables

A two-tailed Spearman's *rho* correlation coefficient was calculated for the relationship between the categorical demographic variables of age groups, gender, race, ethnicity, marital status, employment status, education, insurance, income level, and time posttransplant groups.

A low, negative correlation that was significant (r = -.213, p=.035) was found between age as grouped into younger (≤ 54 yrs) and older (≥ 55 yrs) participants. Older (≥ 55 yrs) transplant recipients were less adherent than younger (≤ 54 yrs) recipients. Table 7 summarizes correlation statistics for all categorical demographic variables.

Table 7 Correlations Between Demographic Characteristics and Composite Adherence Groups

Demographic Variable	*n*	*r*	*p (two-tailed)*
Age group (≤54yrs; ≥ 55yrs)	98	-.213	.035
Gender	98	-.013	.896
Race	98	-.111	.275
Ethnicity	98	.063	.540
Marital status	98	-.129	.207
Education	98	-.048	.638
Insurance	98	-.050	.628
Income	98	-.053	.605
Time posttransplant groups (≤ 5 yrs; ≥ 6 yrs)	98	-.033	.750

* p <.05

Hypothesis 1

Hypothesis 1: There will be a significant negative relationship between the predictor variable of time posttransplant as measured in years and composite adherence group classification.

A one –tailed Spearman's *rho* correlation coefficient was calculated for the relationship between the predictor variable of time posttransplant as measured in years and composite adherence group classification. A weak, negative correlation was found (r = -.053, p=.303). The research hypothesis was rejected. *Time posttransplant was not related to composite adherence group classification.*

Hypothesis 2

Hypothesis 2: There will be a significant relationship between the predictor variable of age as measured in years and composite adherence group classification.

A two-tailed Spearman's *rho* correlation coefficient was calculated for the relationship between the predictor variable of age as measured in years and composite adherence group classification. A weak, negative correlation that was found (r = -.159, p = .118). The hypothesis was rejected. *There was no significant relationship between the predictor variable of age as measured in years and composite adherence group classification.*

Hypothesis 3

Hypothesis 3: There will be a significant relationship between medication complexity index scores and composite adherence group classification.

A two-tailed Spearman's *rho* correlation coefficient was calculated for the relationship between the predictor variable of medication complexity index scores and composite adherence group classification. A weak, negative correlation that was found (r = -.038, p = .711). The hypothesis was rejected. *There was no significant relationship between medication IST complexity index scores and composite adherence group classification.*

Hypothesis 4

Hypothesis 4: There will be a significant difference in IST medication complexity scores between composite adherence group classifications.

IST medication complexity index scores of nonadherent and adherent adult renal transplant recipients were compared using an independent –samples t test. Levene's test for equality of variance (F = .218, p = .641) assured that the variances in scores were equally

distributed. No significant difference was found (t (96) = .283, p=.778). Hypothesis 4 was rejected. *Nonadherent and adherent participants had similar IST complexity scores.* Table 8 summarizes results.

Table 8 Group Differences for IST Medication Complexity Scores-Adherent / Nonadherent

Variable / Group	Minimum	Maximum	*M*	*SD*	*t* (df)	*P**
Nonadherent (*n* =59)	4	72	24.58	11.87	.283(96)	.778
Adherent (*n* =39)	4	42	23.90	11.22		

*$p < .05$

Additional t-test analysis was conducted comparing the mean IST complexity index scores between males and females, younger (≤ 54 yrs) and older (≥ 55 years) participants, and time posttransplant groups as grouped around the mean (≤ 5 yrs posttransplant and 6 yrs or more posttransplant). While no significant differences in complexity scores were found between gender and age groups, the mean IST complexity score of participants 5 years or less posttransplant was significantly lower (m = 22.24, sd = 12.095) than the means scores of participants 6 or more years from transplant (m = 28.56, sd = 9.147). Table 9 summarizes group differences for IST medication complexity index scores.

Table 9 Group Differences for IST Medication Complexity Scores-Gender, Age Groups, Time Posttransplant Groups

Variable / Group	Minimum	Maximum	*M*	*SD*	*t* (df)	*P**
Gender (*N*=98)						
Male (*n*=57)	4	48	22.56	10.84	-1.781 (96)	.078
Female (*n* =41)	4	72	26.73	12.22		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	4	72	24.76	12.45	.353 (96)	.725
≥ 55 yrs (*n* =53)	4	48	23.92	10.86		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	4	72	22.24	12.10	-2.613 (96)	.010
≥ 6 yrs (*n* = 32)	12	48	28.56	28.56		

*$p < .05$

Hypothesis 5

Hypothesis 5: There will be a significant relationship between the predictor variable of health beliefs as measured by the BMQ Necessity and BMQ Concerns subscale score and composite adherence group classification.

A Spearman's *rho* correlation coefficient was calculated for the relationship between BMQ Necessity and BMQ Concerns subscales of the Beliefs About Medicines Questionnaire and composite adherence group classification. A low, positive correlation that was not significant was found between the BMQ necessity subscale ($r = .160$, $p = .116$) and composite adherence group classification. A low, negative correlation that was not significant was found between the BMQ concerns subscale ($r = -.124$, $p = .223$) and composite adherence group classification. Hypothesis 5 was rejected. *Scores on both the BMQ Necessity and BMQ Concerns subscales were not related to composite adherence group classification.*

Hypothesis 6

Hypothesis 6*:* There will be a significant difference in BMQ Necessity subscale scores, BMQ Concern subscale scores, and BMQ Necessity/Concerns Differential scores between composite adherence group classifications.

Independent-samples *t* tests were calculated comparing the mean BMQ Necessity, BMQ Concerns, and BMQ Necessity/Concerns Differential scores between adherent and nonadherent participants. Table 10 summarizes results with the reported *p* values reflective of the Levene's statistic. Hypothesis 6 was rejected as no significant differences were found in scores between groups. The mean scores of nonadherent participants were not significantly different from the mean scores of adherent participants across all BMQ scores.

Table 10 Group Differences for Nonadherent / Adherent Groups-Beliefs About Medicines

Variable / Group	Minimum	Maximum	*M*	*SD*	*t* (df)	*P**
BMQ Necessity (*N* = 98)						
Nonadherent (*n* = 59)	5	25	22.58	4.32	-1.682 (88)	.096
Adherent (*n* = 39)	16	25	23.67	2.02		
BMQ Concern (*N* =98)						
Nonadherent (*n* = 59)	5	23	11.25	3.99	1.049 (96)	.297
Adherent (*n* = 39)	5	20	10.44	3.43		
Necessity / Concerns Differential (*N* =98)						
Nonadherent (*n* = 59)	-1.60	4.00	2.26	1.27	-1.632 (96)	.106
Adherent (*n* = 39)	.00	4.00	2.65	.88		

*$p < .05$

Additional analyses were conducted comparing the mean BMQ scale scores between males and females, younger (≤ 54 yrs) and older (≥ 55 years) participants, and time posttransplant groups (≤ 5 yrs posttransplant and 6 yrs or more posttransplant). Reported *p* values were based on Levene's test for equality of variances. No significant differences in all

scale scores between gender, age groups, and time posttransplant groups were found. Table 11 summarizes results.

Table 11 Group Differences for Gender, Age Groups, Timeposttransplant Groups-Beliefs About Medicines

Group	BMQ Necessity Scale (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	5	25	23.33	3.340	1.046 (96)	.298
Female (*n* =41)	5	25	22.56	3.950		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	5	25	23.38	3.632	.929 (96)	.355
≥ 55 yrs (*n* =53)	5	25	22.70	3.53		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	13	25	23.41	2.683	1.304 (40)	.200
≥ 6 yrs (*n* = 32)	5	25	22.19	4.961		
Group	**BMQ Concern Scale (*N*=98)**					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*p*
Gender (*N*=98)						
Male (*n*=57)	5	23	10.86	3.819	-.212 (96)	.833
Female (*n* =41)	5	20	11.02	3.778		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	5	23	10.67	4.023	-.629 (96)	.531
≥ 55 yrs (*n* =53)	5	20	11.15	3.592		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	5	23	10.92	4.017	-.016 (96)	.987
≥ 6 yrs (*n* = 32)	6	18	10.94	3.311		

*$p < .05$

Group	BMQ Necessity / Concerns Differential (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	-1.600	4.00	2.49	1.09	.799 (96)	.426
Female (*n* =41)	-.800	4.00	2.31	1.22		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	-1.600	4.00	10.67	4.023	1.005 (96)	.318
≥ 55 yrs (*n* =53)	-.600	4.00	11.15	3.592		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	-.800	4.00	2.50	1.09	1.003 (96)	.318
≥ 6 yrs (*n* = 32)	-1.600	3.80	2.25	1.24		

*$p < .05$

Hypothesis 7

Hypothesis 7: There will be a significant positive relationship between the predictor variable of social support as measured by MSSS total and subscale (TAN, POS, EMI, AFF) scores and composite adherence group classification.

A one-tailed Spearman's *rho* correlation coefficient was calculated for the relationship between all MSSS subscale scores and total scale scores and composite adherence group classification. Low, positive correlations that were significant were found between the Tangible Support (TAN) subscale (r = .215, p =.017), Emotional Informational Support (EMI) subscale (r = .274, p = .003), Positive Social Interaction (POS) subscale (r = .199, p = .025), MSSS total scale scores (r = .274, p =.003) and composite adherence group classification. A low, positive correlation that was not significant was found between the Affectionate Support (AFF) subscale (r = .054, p = .297) and composite adherence group classification. The hypothesis was partially accepted. *Participants that were adherent perceived significantly greater tangible, emotional/informational, positive social interaction, and overall social support than nonadherent participants.*

Hypothesis 8

Hypothesis 8: There will be a significant difference in MSSS subscale and total scale scores between composite adherence group classifications.

Independent-samples t tests were calculated comparing all mean MSSS subscale (TAN, POS, EMI, AFF) scores and total MSSS scale scores between adherent and nonadherent participants. Reported p values reflect the Levene's test for equality of variances. A significant difference was found between the mean scores of the EMI subscale (t (96) = -2.491, p =.014),

POS subscale (t (95) = -2.1.06, p =.038), and MSSS total scale scores (t (96) = -2.261, p =.026) and composite adherence group classification. The mean scores of the nonadherent group for emotional, positive social interaction, and total overall social support were significantly lower than the mean scores of adherent participants. Hypothesis 8 was partially accepted. *There was a significant different between the mean scores of the EMI, POS, and MSSS total scale scores for nonadherent and adherent participants*. Table 12 summarizes results.

Table 12 Group Differences for Nonadherent / Adherent Groups-Modified Social Support Scales

Variable / Group	Minimum	Maximum	*M*	*SD*	*t* (df)	*P**
TAN (*N* = 98)						
Nonadherent (*n* = 59)	4	20	16.15	4.326	-1.675 (96)	.097
Adherent (*n* = 39)	4	20	17.59	3.885		
EMI (*N* =98)						
Nonadherent (*n* = 59)	8	40	32.37	7.488	-2.491(96)	.014
Adherent (*n* = 39)	20	40	35.90	5.757		
AFF (*N* = 98)						
Nonadherent (*n* = 59)	4	15	13.51	2.438	-1.143 (95.9)	.256
Adherent (*n* = 39)	8	15	13.97	1.597		
POS (*N* = 98)						
Nonadherent (*n* = 59)	5	15	12.73	2.671	-2.106 (94.7)	.038
Adherent (*n* = 39)	8	15	13.72	1.973		
MSSS total score (*N* = 98)						
Nonadherent (*n* = 59)	7	23	18.69	3.679	-2.261 (96)	.026
Adherent (*n* = 39)	11	23	20.29	3.033		

*p < .05

Additional analyses were conducted comparing the mean MSSS subscale scores (TAN, POS, EMI, AFF) and MSSS total scale scores between males and females, younger (≤ 54 yrs) and older (≥ 55 years) participants, and time posttransplant groups (≤ 5 yrs posttransplant and 6

yrs or more posttransplant). Reported *p* values were based on Levene's test for equality of variances.

While no significant differences were found between the mean scores of age groups and time posttransplant groups, a significant difference between the mean scores of men and women on the TAN subscale (t (64) = 2.842, p = .006), AFF subscale (t (96) = 2.081, p = .040), and MSSS total scale score (t (96) = 2.263, p = .026). The mean TAN, AFF, and MSSS total scale scores for men were significantly higher than women. Table 13 summarizes test results.

Table 13 Group Differences for Gender, Age Groups, Timeposttransplant Groups-Modified Social Support Scales

Group	Tangible Support (TAN) (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	8	20	17.77	3.235	2.842 (64)	.006
Female (*n* =41)	4	20	15.27	4.930		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	4	20	16.07	4.750	-1.407 (81)	.163
≥ 55 yrs (*n* =53)	4	20	17.28	3.613		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	6	20	16.85	3.986	.418 (96)	.677
≥ 6 yrs (*n* = 32)	4	20	16.47	4.656		
Group	**Emotional Informational Support (EMI) (*N*=98)**					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*p*
Gender (*N*=98)						
Male (*n*=57)	20	40	34.65	5.972	1.457 (96)	.148
Female (*n* =41)	8	40	32.56	8.219		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	8	40	32.58	8.341	-1.516 (75)	.134
≥ 55 yrs (*n* =53)	18	40	34.79	5.586		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	8	40	33.74	6.769	-.067 (96)	.947
≥ 6 yrs (*n* = 32)	13	40	33.84	7.671		

*$p < .05$

Group	Affectionate Support (AFF) (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	8	15	14.07	1.657	2.081 (96)	.040
Female (*n* =41)	4	15	13.17	2.616		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	4	15	13.24	2.723	-1.847 (64)	.069
≥ 55 yrs (*n* =53)	10	15	14.08	1.412		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	4	15	13.73	2.094	.220 (96)	.826
≥ 6 yrs (*n* = 32)	5	15	13.63	2.282		

Group	Positive Social Interaction (POS) (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*p*
Gender (*N*=98)						
Male (*n*=57)	7	15	13.49	2.180	1.773 (96)	.079
Female (*n* =41)	5	15	12.61	2.737		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	5	15	12.82	2.933	-1.082 (74)	.283
≥ 55 yrs (*n* =53)	9	15	13.38	1.954		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	5	15	13.00	2.542	-.707 (96)	.481
≥ 6 yrs (*n* = 32)	6	15	13.38	2.282		

*$p < .05$

	MSSS Total Scale Score (*N*=98)					
Group	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	11	23	20.00	2.910	2.263 (96)	.026
Female (*n* =41)	7	23	18.40	4.063		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	7	23	18.68	4.223	-1.650 (72)	.103
≥ 55 yrs (*n* =53)	12	23	19.88	2.686		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	7	23	19.33	3.408	.002 (96)	.999
≥ 6 yrs (*n* = 32)	9	23	19.33	3.769		

*$p > .05$

Hypothesis 9

Hypothesis 9: There will be a significant negative relationship between the predictor variable of symptom experience as measured by MTSOSD-59R total ridit scores and composite adherence group classification.

A one-tailed Spearman's *rho* correlation coefficient was calculated for the relationship between total ridit scores for MTSOSD-59R Symptom Occurrence and Symptom Distress scales and composite adherence group classification. A low negative correlation that was not significant was found (r = -.162, p = .055) for the relationship between Symptom Frequency total ridit scores and composite adherence group classification. A low, negative correlation that was also not significant was found (r = -.143, p =.081) between Symptom Distress total ridit scores and composite adherence group classification. Hypothesis 9 was rejected. *There was no significant relationship between symptom experience and composite adherence group classification*. Table 14 identifies by rank order, the most prominent symptoms and associated distress experienced by gender, age, time posttransplant, and adherence groups.

Additional analyses were conducted to determine the relationship between individual symptoms and composite adherence group classification. Three symptoms demonstrated a significant relationship with composite adherence group classification. Dizziness (r = .288, p =.037), difficulty concentrating and / or memory problems (r = -.327, p =.016), and chest pain (r = -.471, p =.036) demonstrated significant relationships with adherence group classification. *Adherent participants experienced significantly less chest pain, dizziness, and difficulty concentrating or memory problems*.

Table 14 Symptom Distress-Gender, Age, Time Posttransplant, Adherence

Gender (*N* = 98)								
Symptoms*	**Prevalence *n* (%)**	**Not Distressing**				**Distressing**			
		Males		**Females**		**Males**		**Females**	
		n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Tiredness	65 (66.3)	13	41.9	12	35.3	18	58.1	22	64.7
Wind	61 (62.2)	17	51.5	9	32.1	16	48.5	19	67.9
Lack of Energy	59 (60.2)	11	32.4	5	20	23	67.6	20	80
Bruise Easy	57 (58.2)	9	33.3	5	16.7	18	66.7	25	83.3
Joint Pain	56 (57.1)	11	34.4	9	37.5	21	65.6	15	62.5
Restlessness / Nervousness	56 (57.1)	3	9.7	4	16.0	28	90.3	21	84
Concentration / Memory Problems	54 (55.1)	13	40.6	9	40.9	19	59.4	13	59.1
Dizziness	53 (54.1)	3	10.7	3	12	25	89.3	22	88
Sleep Difficulties	52 (53.1)	5	16.7	10	45.5	25	83.3	12	54.5
Muscle Weakness	47 (48.0)	4	16.0	5	22.7	21	84	17	77.3

Note: Rank order of the first 10 most prominent symptoms and associated distress by gender.

Age (*N* = 98)								
Symptoms*	**Prevalence *n* (%)**	**Not Distressing**				**Distressing**			
		≤ 54 yrs		**≥ 55 yrs**		**≤ 54 yrs**		**≥ 55 yrs**	
		n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Tiredness	65 (66.3)	12	42.9	13	35.1	16	57.1	24	64.9
Wind	61 (62.2)	10	40	16	44.4	15	60	20	55.6
Lack of Energy	59 (60.2)	5	19.2	11	33.3	21	80.8	22	66.7
Bruise Easy	57 (58.2)	7	5.6	7	8.4	16	69.6	27	47.4
Joint Pain	56 (57.1)	9	39.1	11	33.3	14	60.9	22	66.7
Restlessness / Nervousness	56 (57.1)	1	4.3	6	18.2	22	95.7	27	81.8
Concentration / Memory Problems	54 (55.1)	12	60	10	29.4	8	40	24	70.6
Dizziness	53 (54.1)	2	9.5	4	12.5	19	90.5	28	87.5
Sleep Difficulties	52 (53.1)	5	21.7	10	34.5	18	78.3	19	65.5
Muscle Weakness	47 (48.0)	6	28.6	3	11.5	15	71.4	23	88.5

Note: Rank order of the first 10 most prominent symptoms and associated distress by age.

Time Posttransplant (*N* = 98)									
Symptoms*	**Prevalence *n* (%)**	**Not Distressing**				**Distressing**			
		≤ 5 yrs posttransplant		**≥ 6 yrs posttransplant**		**≤ 5 yrs posttransplant**		**≥ 6 yrs posttransplant**	
		n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Tiredness	65 (66.3)	16	38.1	9	39.1	26	61.9	14	60.9
Wind	61 (62.2)	17	45.9	9	37.5	20	54.1	15	62.5
Lack of Energy	59 (60.2)	12	28.6	4	23.5	30	71.4	13	76.5
Bruise Easy	57 (58.2)	8	22.2	6	28.6	28	77.8	15	71.4
Joint Pain	56 (57.1)	16	42.1	4	22.2	22	57.9	14	77.8
Restlessness / Nervousness	56 (57.1)	3	8.1	4	21.1	34	91.9	15	78.9
Concentration / Memory Problems	54 (55.1)	13	38.2	9	45	21	61.8	11	55
Dizziness	53 (54.1)	5	14.3	1	5.6	30	85.7	17	94.4
Sleep Difficulties	52 (53.1)	11	32.4	4	22.2	23	67.6	14	77.8
Muscle Weakness	47 (48.0)	9	29	0	0	22	71	16	100

Note: Rank order of the first 10 most prominent symptoms and associated distress by time posttransplant.

Adherence (*N* = 98)								
Symptoms*	**Prevalence *n* (%)**	**Not Distressing**				**Distressing**			
		Nonadherent		**Adherent**		**Nonadherent**		**Adherent**	
		n	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Tiredness	65 (66.3)	14	32.6	11	50	29	67.4	11	50
Wind	61 (62.2)	16	42.1	10	43.5	22	57.9	13	56.5
Lack of Energy	59 (60.2)	10	27.8	6	26.1	26	72.2	17	73.9
Bruise Easy	57 (58.2)	11	28.2	3	16.7	28	71.8	15	83.3
Joint Pain	56 (57.1)	16	40	4	25	24	60	12	75
Restlessness / Nervousness	56 (57.1)	4	10.8	3	15.8	33	89.2	16	84.2
Concentration / Memory Problems	54 (55.1)	12	30.8	10	66.7	27	69.2	5	33.3
Dizziness	53 (54.1)	1	3.3	5	21.7	29	96.7	18	78.3
Sleep Difficulties	52 (53.1)	10	27	5	33.3	27	73	10	66.7
Muscle Weakness	47 (48.0)	7	21.9	2	13.3	25	78.1	13	86.7

Note: Rank order of the first 10 most prominent symptoms and associated distress by adherence.

Hypothesis 10

Hypothesis 10: There will be a significant difference in MTSOSD-59R total ridit scores between composite adherence group classifications.

An independent-samples *t* test was calculated comparing the mean MTSOSD-59R Symptom Frequency and Symptom Distress total ridit scores of nonadherent and adherent long-term adult renal transplant recipients. No significant difference was found between groups for both Symptom Frequency total ridit scores (t (96) = 1.704, p = .092) and Symptom Distress total ridit scores (t (96) = 1.232, p = .221). *The mean scores of adherent participants were not significantly different from nonadherent participants for both the MTSOSD-59 R Symptom Frequency and Symptom Distress total ridit scores.* Table 15 summarizes group scores.

Table 15 Group Differences Nonadherent / Adherent-MTSOSD-59R Symptom Occurrence and Symptom Distress Total Ridit Scores

Variable / Group	Minimum	Maximum	*M*	*SD*	*t* (df)	*P**
MTSOSD-59R Symptom Frequency						
Nonadherent (*n* = 59)	20.57	41.62	30.64	5.82	1.704 (96)	.092
Adherent (*n* = 39)	19.10	43.46	28.54	6.17		
MTSOSD-59R Symptom Distress						
Nonadherent (*n* = 59)	1.77	24.46	10.42	5.90	1.232 (96)	.221
Adherent (*n* = 39)	.000	32.42	8.88	6.35		

*$p < .05$

Additional analyses were conducted comparing the means of Symptom Frequency and Symptom Distress total ridit scores between males and females, younger ($\leq$ 54 yrs) and older ($\geq$ 55 years) participants, and time posttransplant groups ($\leq$ 5 yrs posttransplant and 6 yrs or more posttransplant). The reported p value reflected the Levene's statistic. No significant difference in mean scores was found between groups. Table 16 summarizes results.

Table 16 Group Differences Gender, Age Groups, Time Posttransplant Groups-MTSOSD-59R Symptom Occurrence and Symptom Distress Total Ridit Scores

Group	MTSOSD-59R Symptom Frequency (*N*=98)					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*P**
Gender (*N*=98)						
Male (*n*=57)	19.11	42.09	28.96	6.01	-1.647 (96)	.103
Female (*n* =41)	20.57	43.46	30.98	5.91		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	19.11	42.09	30.03	6.39	.345 (96)	.731
≥ 55 yrs (*n* =53)	20.57	43.46	29.61	5.74		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	19.10	42.09	29.66	6.21	-.349 (96)	.728
≥ 6 yrs (*n* = 32)	20.24	43.46	30.11	5.68		
Group	**MTSOSD-59R Symptom Distress (*N*=98)**					
	Minimum	Maximum	*M*	*SD*	*t*(df)	*p*
Gender (*N*=98)						
Male (*n*=57)	.000	30.42	9.37	6.13	-.831 (96)	.408
Female (*n* =41)	1.56	24.46	10.41	6.07		
Age (*N* =98)						
≤ 54 yrs (*n*=45)	.000	30.42	9.83	6.96	.037 (81)	.970
≥ 55 yrs (*n* =53)	1.56	24.22	9.78	5.32		
Time posttransplant (*n* = 98)						
≤ 5 yrs (*n* = 66)	.000	30.42	10.18	6.61	.862	.391
≥ 6 yrs (*n* = 32)	1.77	17.65	9.04	4.86		

*$p < .05$

Logistic Regression Analysis

To answer the primary research question of which of six predictor variables demographic variables, time since transplant, immunosuppressive agents, health beliefs, social support, and symptom experience are most influential in predicting IST adherence in long-term adult renal transplant recipients, a forward logistic regression was conducted. Predictor variables demonstrating a significant relationship to adherence (age groups, TAN subscale, POS subscale, EMI subscale, and MSSS total scale scores) were entered into the final logistic regression analysis.

Prior to analysis, data were explored for missing values and outliers. Preliminary multiple linear regression analysis was conducted to calculate Mahalanobis distance and to evaluate multicollinearity. Initial results indicated multicollinearlity was violated as tolerance statistics were less than .1 for all social support scales. To address this problem, the independent variable of MSSS total scale score was removed. The resultant table of regression coefficients (see Table 18) indicated multicollinearity was not violated since tolerance statistics for all three independent variables were greater than 0.1. Data were explored to determine which cases exceeded the Mahalanobis distance critical value of x^2 (3) = 16.266 at p = .001. One subject exceeded this value (case #86) and was eliminated from analysis.

Table 17 Collinearity Statistics

Variable	Collinearity Statistics	
	Tolerance	VIF
(TAN)Tangible Support Subscale	.587	1.705
(EMI) Emotional Informational Support Subscale	.297	3.366
(POS) Positive Social Interaction Subscale	.366	2.732

Binary logistic regression using the Forward: LR method was then conducted to determine which independent variables (age [≤ 54 yrs, ≥ 55 yrs], TAN subscale, EMI subscale, POS subscale) were predictors of adherence group classification (adherent/nonadherent). Regression results indicated the overall model of two predictors (age [≤ 54 yrs, ≥ 55 yrs] and EMI subscale) was statistically reliable in distinguishing between adherent and nonadherent participants (-2 Log Likelihood 116.244; Goodness-of-Fit x^2 (2) = 13.664, p = .001). The model correctly classified 69.1% of the cases. Regression coefficients are presented in Table 18. *Wald* statistics indicated that age (< 54 yrs, > 55 yrs) and EMI subscale significantly predicted adherence group classification. Odds ratios for the EMI (e^B = 1.105) variable indicated that as the variable EMI increases by 1, participants were 1.105 times more likely to be classified as adherent. Odds ratio for the variable age grouped (e^B = 3.320) indicated that as age grouped increased by 1, participants were 3.320 times as likely to be classified as adherent.

Table 18 Regression Coefficients

	B	*Wald*	d*f*	*p*	Odds Ratio	95% Confidence Interval	
						Lower	Upper
EMI (Emotional / Informational) subscale	.100	7.028	1	.008	1.105	1.026	1.189
Age group (≤ 54 yrs; ≥ 55 years)	1.200	6.871	1	.009	3.320	1.354	8.144
Constant	-4.435	10.142	1	.001			

Summary

The results of this study demonstrated weak, but significant relationships between age group, TAN subscale, POS subscale, EMI subscale, and MSSS total scale scores and adherence group classification. While perceived emotional and information social support and being older significantly predicted adherence, odds ratios demonstrated moderate change in the likelihood of adherence on the basis of a one unit change in age or perceived emotional/informational support. Thus, age and perceived emotional/informational support distinguished moderately between nonadherent and adherent long-term adult renal transplant recipients.

CHAPTER FIVE: DISCUSSION

During the past ten years, many studies have explored predictors of immunosuppressant (IST) medication adherence in adult renal transplant recipients. To date, this is the first study to examine predictors of IST medication adherence in a population of long-term renal transplant recipients. The purpose of this study was to examine demographics, time posttransplant, immunosuppressive agents, health beliefs, social support, and symptom experience and test their relationship to IST adherence based upon the Health Decision Model as adapted by the principal investigator for use in this study. This chapter compares and contrasts study findings with results reported in previous research. Implications for nursing practice as well as recommendations for future research are discussed.

Sample

While the sample in this study was similar to the U.S. renal transplant population as reported by the Organ Procurement Transplant Network (2009), study findings should not be generalized to the entire population. This study sample was similar to the U.S. renal transplant population in terms of gender (58.2% men versus 60.4% nationally). Age group distributions indicated a slightly older population in this study (see Table 19). Finally, while African Americans were appropriately represented (27.6% versus 25.7% nationally), Asian and "other" race categories were underrepresented.

Table 19 Comparison of Study Participants and U.S. Transplant Population

Characteristic	Study (%)	U.S. Transplant Population (%)
Age		
18-34	6.1%	13.8%
35-49	17.3%	28.4%
50-64	46.9%	41.1%
65+	29.6%	16.7%
Gender		
Male	58.2%	60.4%
Female	41.8%	39.6%
Race		
White	70.4%	53.4%
Black	27.6%	25.7%
Asian	2%	5.5%
Other / unknown	0%	1.3%
Ethnicity		
Hispanic	18.2%	14.2%

Adherence

Though healthcare providers in this study setting considered long-term recipients generally adherent, 60.2% of this study's participants were nonadherent to their immunosuppressant medications when defined as older ($\geq$ 55 yrs) in this study. Variations in methods of measuring IST adherence have contributed to the wide range of previously reported adherence rates. When measured by self-report methods, IST adherence is often overestimated (Osterberg & Blaschke, 2005). In contrast, a study by Russell et al. (2010) noted that use of a self-report measure of adherence that captures timing adherence behaviors may contribute to an overall low percentage of adherent participants in a sample where 86% of older renal transplant recipients were identified as being nonadherent. Results from this study yielded similar findings.

One study to date has used a composite score of adherence, similar to the one used for this study. The composite score, used by Schmidt-Mohler et al. was composed of clinician collateral reports and the same self-report measure used in this study (BAASIS) which captures timing adherence (Schmid-Mohler, Thut, Wüthrich, Denhaerynck, & De Geest, 2010). Authors of this study categorized participants as adherent, partially adherent, or nonadherent. However, if findings were dichotomized, 76% of the sample would have been classified as nonadherent (partially adherent or nonadherent). Results from this study yielded a similarly high rate of nonadherence.

Age

The majority of studies have reported younger age as being associated with nonadherence (Chisholm-Burns, Kwong, Mulloy, & Spivey, 2008; M. A. Chisholm, Lance, & Mulloy, 2005; Denhaerynck et al., 2007; Frazier, Davis-Ali, & Dahl, 1994; Ghods, Nasrollahzadeh, & Argani, 2003; Greenstein & Siegal, 1998; Gremigni et al., 2007). Of these studies, few have clearly defined younger and older age categories. In this study, age was assessed both as a continuous variable and older/younger categorical variable. While findings from this study failed to correlate age (continuous variable) with adherence, a significant, low negative correlation was found when grouping participants into older and younger age groups. Older transplant recipients ($\geq$ 55 yrs) were identified as being less adherent than younger participants ($\leq$ 54 yrs). Recent studies defining "older" age groups yielded similar results with Chisholm-Burns et al. (2008) reporting adherence as being lower among recipients 60 or more years of age and Russell et al. (2011) reporting significant nonadherence (86%) in recipients 55 years of age or older.

Time Posttransplant

The mean time posttransplant for participants in this study was 4.95 yrs. Analysis failed to support a significant relationship between time posttransplant and adherence. Findings from this study contrast with the majority of studies that reported increased time from transplant as being significantly associated with nonadherence (Chisholm-Burns, et al., 2008; Chisholm, et al., 2005; Chisholm, Mulloy, & DiPiro, 2005; Greenstein & Siegal, 1998; Ichimaru et al., 2008). While earlier research findings support an inverse relationship between time posttransplant and adherence to IST medications, one study to date has defined time posttransplant quartiles in an effort to isolate the most useful time posttransplant to reinforce adherence. Chisholm-Burns et al. (2008) concluded that recipients who were 4 years or less from transplant had higher overall adherence to immunosuppressive medications than those 5 or more years from transplant identifying a useful point for targeted interventions by healthcare providers. Both the frequency of medication adjustments and follow-up appointments that occur during the first two years following transplant could explain these findings. Given the lack of association between time posttransplant (m=4.95 yrs) and adherence in this study, the quality of long-term primary care provided by both the local primary care providers and the transplant clinic could be a possible factor influencing long-adherence. Additionally, limited research has explored the effect of comorbidities and their associated treatments (e.g. more medications) on IST adherence. The burden of treating concomitant chronic conditions that increase with age may also be a factor.

IST Medications

A calculated medication complexity index score (number of medications x number of IST pills taken per day x number of times per day taking IST medications) was used to determine the relationship between IST medications and adherence. Although no study to date conducted within the adult renal transplant population has used this method of measure, all components of the measure have been used either alone or in combination in many previous studies. Using this method of measure, nonadherent participants were found to have a higher mean IST complexity index score (*m*=24.58) than adherent participants (*m*=23.90), but the difference was not statistically significant. In addition, study findings failed to find a significant relationship with adherence. Results from previous studies are mixed (Goldfarb-Rumyantzev et al., 2011; Schmid-Mohler, et al., 2010; Sketris et al., Vasquez, Tanzi, Benedetti, & Pollak, 2003; Weng et al., 2005) with several factors providing possible explanations. While this study included only IST medications in the analysis, other studies included either all prescribed medications or did not clearly indicate which medications were used in the final analysis. In addition, the types of medications, dosing frequencies, and medication regimens (combination or triple therapy) used in previously reported studies reflected those represented in this study. However, the method or combination of methods used to measure the dependent variable of adherence varied across all studies. Finally, included in many study samples were participants in the immediate posttransplant period (first 6 months) up to as few as 1-2 years posttransplant; the times during which doses are frequently adjusted and/or medications weaned off and discontinued (Prednisone) both of which can influence dosing complexity.

Beliefs About Medicines

Findings from this study failed to support a significant relationship between beliefs about medicines and adherence. These results are in contrast to those reported by Butler et al. (2004) who concluded a lower belief in the need for medications was associated with nonadherence. While results from this study indicated nonadherent participants has lower beliefs in the need for medicines as reported by the mean Necessity scale score (m= 22.58 nonadherent versus m=23.67 adherent), the results failed to achieve statistical significance. One possible explanation for this failure was the presence of a nonnormal distribution as influenced by Necessity scale score outliers.

Additional study findings not achieving statistical significance in this study, may be of clinical significance to healthcare providers. As compared to younger ($\leq$ 54 yrs) participants, older participants ($\geq$ 55 yrs) had lower beliefs in the need for medicines and greater concerns over the consequences of taking medicines. In addition, females demonstrated lower beliefs in the need for medicines yet greater concern over the consequences of taking medicines. While concerns over the consequences of taking medicines were virtually the same in both time posttransplant groups ($\leq$ 5 yrs, $\geq$ 6 yrs), participants six or more years from transplant reported lower beliefs in the need for medicines, which ultimately could influence adherence.

Social Support

Limited studies have explored social support within the context of IST adherence in the adult renal transplant population. Of those that have, results have been mixed. Using the Social Support Appraisal Index, a 23 item scale that measures the degree to which a person feels cared

for, respected, and involved with family and friends, Russell et al. (2010) reported no significant relationship between social support and IST adherence in a population of older (≥ 55 years) recipients.

Using the shorter 5 item version of the Modified Social Support Scale (MSSS), Chisholm-Burns et al. (2010) reported a significant relationship between social support and IST adherence with affectionate support and an instrumental support item (help with household functions) as being associated with total adherence summary scores. Of note in the Chisholm-Burns et al. (2010) study was the reported mean age (m =48.9) of the sample.

Findings reported in this study, using the 18 item MSSS scale, mirrored findings reported by Chisholm-Burns et. al. (2010) noting a significant relationship between social support and increased adherence. However, contrary to findings reported by Chisholm-Burns et. al. (2010), results from this study did not support a significant relationship between affectionate support subscale items and adherence. One possible explanation for this finding could be the higher overall percent of participants in this study that reported being married or living together (70.4%) versus the lower percent of married participants in the Chisholm-Burns et. al. (2010) study (28.7%).

Symptom Experience

Results obtained in this study failed to demonstrate a significant relationship between symptom experience and adherence as measured by total overall symptom frequency and symptom distress total ridit scores. In addition, results comparing differences in age, gender, time posttransplant, and adherence groups failed to achieve significant levels despite the overall

normal distribution of both symptom frequency and symptom distress total ridit scores. While reported findings were not statistically significant, results comparing differences in groups may be of clinical significance to healthcare providers.

It is important to note that no study to date has explored the relationship between symptom experience and adherence using the updated MTSOSD-59R instrument reflective of current IST regimens. In addition, of the studies exploring the effect of symptom experience on adherence, all have been conducted within European or Canadian populations (Butler et al., 2004; Denhaerynck et al., 2007; Sketris et al., 1994; Teixeira De Barros & Cabrita, 1999). This study is the first to obtain data from a U.S. sample.

Findings reported in this study noted higher mean overall symptom frequency [nonadherent (m = 30.64), adherent (m = 28.54)] and symptom distress ridit scores [nonadherent (m =10.42), adherent (m = 8.88)] in nonadherent participants, though results were not significant. A study conducted by Teixeira De Barros and Cabrita (1999) in a population of Portuguese renal transplant recipients using the MTSOSD 45 item scale reported similar results with significantly higher overall symptom frequency and symptom distress ridit scores in nonadherent participants. Perhaps the failure to achieve statistical significance in this study is due to possible cultural variations in the measured level of symptom experience.

Age related findings reported in this study were in contrast to those reported by Teixeira De Barros et al. (1999) who identified significantly higher mean symptom frequency scores in older participants ($\geq$ 40 yrs). Findings reported in this study noted younger participants ($\leq$ 54 yrs) as having higher, though nonsignificant, overall mean symptom frequency scores. Mean symptom distress scores were essentially the same in this study between age groups mirroring

similar findings in the study by Teixeira De Barros et al. (1999). Cultural variations, variations in IST regimens, instruments versions used to measure symptom experience, and variations in defined age groups are all factors possibly influencing conflicting results.

Finally, no study to date has explored differences in symptom experience between groups based on time posttransplant. Results in this study noted participants who were six or more years from transplant had lower, though nonsignificant, mean symptom distress scores and higher mean symptom frequency scores than participants who were 5 years or less from transplant. Perhaps the higher mean symptom frequency scores found in those participants 6 or more years from transplant is due to the development of symptoms similar to those associated with IST therapy but also associated with comorbid conditions that can develop as a result of long-term IST therapy (diabetes, hypertension). Conversely, perhaps the lower mean symptom distress scores found in the same time posttransplant group ($\geq$ 6 yrs time posttransplant) can be attributed to tolerance or lessening of the intensity of symptom distress over time. Research in this area is nonexistent. Further research within the context of current immunosuppressive regimens is warranted.

Implications

Findings reported in this study add to the body of knowledge concerning IST adherence in adult renal transplant recipients by focusing on a population defined as long-term. While results from this study have implications for nursing education, practice, and policy, the greatest implications lie within nursing practice.

Nursing Practice

Of the 96,918 patients currently awaiting renal transplantation in the United States, 41,678 (43%) of those awaiting transplant are between 50 and 64 years of age (OPTN, 2012). Results of this study demonstrate a negative correlation between age groups and adherence with older ($\geq$ 55 yrs) participants being less adherent than younger participants. Given the higher percentage of nonadherent participants in this study (60%) and the mean age of participants in this study (57.19 yrs), multidisciplinary teams providing care for long-term transplant recipients may want to consider the findings in this study and implement both adherence screening measures as well as interventions directed at modifiable variables associated with adherence in this age group.

Nurses and advanced nurse practitioners working in outpatient clinic settings, may consider screening patients in this age group annually for nonadherence by using a feasible measure of self-report such as the BAASIS. Nurses could educate patients screened as nonadherent about the use of reminder methods to enhance adherence (e.g. pillboxes, storing medications with other items associated with daily rituals, keeping medications in the same location). In addition, if medication complexity involving IST medications as well as medications for other comorbid conditions is high, nurse practitioners collaborating with nephrologists could review regimens in an effort to simplify medication dosing regimens to promote better adherence.

Emotional/information social support, consisting of physical comforting, listening, and empathizing along with the giving of advice and sharing information, was statistically reliable in distinguishing between adherers and nonadherers. Considering the potential for change in social

support networks over the lifespan, licensed social workers as members of a multidisciplinary team could be involved in both screening for changes in social networks in this age group as well as integral in facilitating appropriate interventions.

For nonadherent patients demonstrating a lack of perceived emotional/informational social support systems, a few interventions may be considered. The use of support groups is common during the pretransplant phase of care to aid patients in determining if transplantation as a therapy is an appropriate choice. Continuing these same support group sessions during the posttransplant phase of care may provide recipients who are experiencing changes in social support networks with a group of individuals able to provide relevant advice and information during times of need.

Policy

The major focus of public policy addressing IST medication adherence in adult renal transplant recipients is on extending lifetime Medicare coverage for costs related to IST therapy to those patients receiving Medicare benefits for reasons other than disability. The results of this study do not contribute to those policy initiatives.

While not public policy, findings from this study could be used to influence national standards of care for kidney transplant recipients. Current Kidney Disease: Improving Global Outcomes (KDIGO) practice guidelines for the care of kidney transplant recipients calls for preventing, detecting, and treating nonadherence (Kasiske, Zeier, Chapman, Craig, Ekberg et al., 2009). Given the relationship between social support and adherence, providing a measure for ongoing screening for changes in social support systems as part of assessing for risk of

nonadherence may be of value in primary care settings. Findings also support the need for more research funds to support the study of adherence in recipients in the United States.

Nursing Education

Results reported in this study may encourage both entry level and advanced practice nursing education programs to incorporate content addressing the impact social support has on adherence in long-term renal transplant recipients. More importantly, as part of ongoing support and care provided over the lifespan of the transplant recipient, both the patient and family should be periodically assessed for changes in social support structure as well as educated on the importance of sustained social support and its relationship to adherence. Nurses also need information on IST medications to better assist in patient teaching and follow-up care. Necessary IST medication information such as drug-to-drug interactions, food-drug interactions, side-effects, timing medications to sustain therapeutic blood levels, and therapeutic drug monitoring should be a part of pharmacology content. Finally, advanced practice registered nurses should stay alert to emerging research addressing once daily dosing regimens that may be of benefit to patients struggling with adherence or those with highly complex medication regimens.

Study Limitations

While an appropriate theoretical basis, reliable scale instruments, data collection methods, and an adequate sample size added strength to the study, several limitations of this study were evident and are discussed separately.

Limitations related to the sample include the use of a convenience sample and associated cross sectional design. Given the demographic differences between the sample population and the U.S. transplant population (see Table 19), results may not be generalizable. Use of a cross sectional design limits the assessment of adherence to one point in time. Given the opinion that all patients are believed to be nonadherent to medication therapy at some point in time, use of this design may fail to adequately represent overall adherence rates. However, given the high percentage of nonadherent participants in this study (60.2%), this is most likely a minimal limitation.

The self-report measure of adherence used in this study represents all dimensions of medication taking behavior including timing. Of the participants in this study, 35.7% were nonadherent with taking medications within 2 hours of the prescribed time. By classifying participants with timing nonadherence as partially adherent, another dimension is represented that may be amenable to intervention. Dichotomizing adherence results in loss of the dimensionality of the concept.

Limitations are also associated with the components making up the composite score of adherence (CAS) used in measure IST adherence in this study. The self-report measure of adherence (BAASIS) used as a component of this study's CAS, runs the risk of under-reporting nonadherence as participants may have felt compelled to answer in a manner viewed as positive by the investigator. Given the high rate of self-reported nonadherence (41.8%) as measured by this instrument, this is also most likely a minimal limitation.

Another component of the CAS, clinician collateral reports, were provided by two transplant clinicians with little knowledge of the medication taking behaviors of participants

beyond the date of their annual clinic appointment. In addition, when asked face-to-face by clinicians if they are having difficulty taking or getting IST medications (the standard clinic adherence assessment in this study setting) participants may be fearful of answering truthfully. However, given the observed interactions between clinical professionals and study participants as well as other clinic patients, this factor is also felt to be of minimal limitation to this study.

The final component of the CAS score used in this study was the serum drug assay. In a study assessing the diagnostic accuracy of measurement methods assessing adherence in renal transplant patients, the CAS score identified as demonstrating 72.1% specificity in detecting nonadherence assessed serum drug assay variability over several serum drug assay values (Schäfer-Keller, Steiger, Bock, Denhaerynck, & De Geest, 2008). The use of a single serum drug assay value versus assessing variability over several trough results may have resulted in the inappropriate classification of participants with isolated nontherapeutic values as nonadherent. This factor is believed by the author to be a major limitation of this study.

Recommendations for Future Research

Serving as the basis for all future research recommendations is the need for investigators to continue to explore factors identified as influencing IST adherence within the context of more consistently defined age and time posttransplant groups. As the adult renal transplant population lives longer and continues to age, the influence of modifiable factors impacting adherence may change over the lifespan of the recipient. By intentionally and consistently defining age groups and time posttransplant intervals, relevant interventions may be more intently targeted during long-term primary care of the adult renal transplant recipient.

Given the conflicting research findings regarding the influence of IST medications (dosing complexity) on adherence, further research is warranted. Future research should not only explore medication complexity associated with IST medications, but also adherence related to other prescribed medications necessary to sustain the health of transplanted grafts (antivirals, antihypertensives, hypoglycemic agents, antibiotics). As both time from transplant and the risk for the development of comorbidties associated with long-term IST therapy increases adherence to such agents becomes just as critical. The potential addition of these additional prescribed medications adds to the complexity of IST regimens which may increase the risk for nonadherence.

While research regarding the influence of symptom experience on adherence in European transplant recipients is available, lacking are studies conducted within a representative sample of the U.S. transplant population. In addition, further analysis of these studies could help formulate symptom profiles specific to IST regimens, gender groups, and ethnic groups.

Finally, given the lack of significant findings related to modifiable variables known to influence adherence (health beliefs), research exploring the influence of the healthcare system (transplant clinic, primary care setting) on adherence.

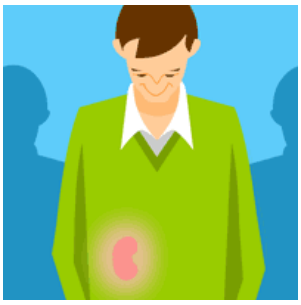
Summary and Conclusion

The purpose of this study was to examine demographics variables, time posttransplant, immunosuppressive agents, health beliefs, social support, and symptom experience and test their relationship to adherence. Using a cross sectional design, a convenience sample of 98 long- term adult renal transplant recipients provided data for this study.

The results of this study added to the current body of knowledge in the area of IST adherence in adult renal transplant recipients. Findings from this study can be used to aid healthcare personnel involved in the long-term care of adult renal transplant recipients in identifying patients at risk for nonadherence. In addition, given the modifiable nature of social support, found to be significantly associated with adherence in this study, healthcare personnel can implement interventions appropriate to support participants experiencing lower perceived social support.

Future research should continue to explore variables known to influence adherence within the context of consistently defined age and time posttransplant groups. By consistently defining groups, cut points could be delineated identifying more focused age groups and time posttransplant intervals amenable to interventions designed to enhance adherence and improve long-term outcomes.

APPENDIX A: RECRUITMENT FLYER



Invitation to Participate in Research

Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients

Desired Participants: Kidney transplant recipients, age 18 at the time of transplant.

Research Purpose: To learn about taking anti-rejection medication after kidney transplant.

Participant Commitment: You are being asked to complete five short, confidential surveys on the day of your annual clinic appointment. There is no cost to you. All participants will be compensated $25.00 per session.

PARTICIPATION IS LIMITED!

Please notify the clinic receptionist if you are interested in participating in this study.

APPENDIX B: IRB DOCUMENTS

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Exempt Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Sandra J. Galura**

Date: **March 29, 2010**

Dear Researcher:

On 3/29/2010, the IRB approved the following activity as human participant research that is exempt from regulation:

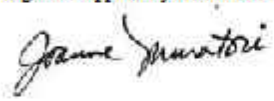
Type of Review:	Exempt Determination
Project Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Investigator:	Sandra J Galura
IRB Number:	SBE-10-06848
Funding Agency:	Sigma Theta Tau International
Grant Title:	Grant Application Pending
Research ID:	N/A

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these changes affect the exempt status of the human research, please contact the IRB. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Joseph Bielitzki, DVM, UCF IRB Chair, this letter is signed by:

Signature applied by Joanne Muratori on 03/29/2010 12:45:50 PM EST



IRB Coordinator

FLORIDA HOSPITAL
601 East Rollins Street
Orlando, FL 32803

To: Sandra Galura, MSN, RN, CCRN, CPAN
Principal Investigator

From: M. Lindell Joseph, PhD, RN
Research Team Leader, Nursing Scientific Review Board

Date: March 12, 2010

Subject: Scientific Clearance for *Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients*. Project, FH#2453-1850.

This memo serves to inform you that the Nursing Scientific Review Board (NSRB) has reviewed and approved the above-named study. The NSRB looks forward to hearing a presentation of your study findings within six months following the completion of your project.

Should you have any questions, please contact me by calling 407-200-2555, Option 5.

Sincerely,

M. Lindell Joseph, PhD, RN

cc: Michelle Dolske, PhD
Administrative Director, Office of Research Administration

Florida Hospital
Institutional Review Board
212 E. Winter Park Street
Orlando, FL 32804
Telephone: (407) 303-5581
Fax: (407) 303-3638
FWA: 00002060

June 3, 2010

Sandra Galura MSN, RN, CCRN
Nursing Research & Innovation
2312 Montana Street
Orlando FL 32803

Dear Ms. Galura:

FH #: 2453-1850; UCF Student Research
Title: Predictors of Immunosuppressant Adherence in Long-Term Renal Transplant Recipients

Florida Hospital IRB Expedited Initial Approval Date: 06.03.10
FH IRB Expiration Date: 05.10.11
Informed Consent/Authorization Approval Date: 06.03.10
Informed Consent may not be used to enroll new subjects beyond: * 05.10.11
Meeting Date for FH IRB Notification: 07.13.10
NOTE: This study may not be initiated without approval of the Florida Hospital Office of Research Administration.

In response to your request and on behalf of the Florida Hospital IRB, the IRB granted expedited approval to the study as noted above, based on categories approved in 21 CFR 56.110 and 45 CFR 46.110. Unless the informed consent requirement was waived, you are required to use the IRB approved informed consent. **The Florida Hospital IRB has approved the above noted informed consent/authorization for use. * Note: should the informed consent be revised, it must be approved by the IRB prior to use and will supersede the above noted approved consent/authorization.**

Prior to the expiration dated noted above, the IRB must be made aware of the status of your project(s). A progress report will be required. [21 CFR 56.109 (f)] If the project has not been completed, you may request renewed approval.

It is your responsibility to remain in compliance with all applicable state and federal regulations regarding research as well as adhering to the Florida Hospital IRB ***Handbook for the Protection of Human Research Subjects.***

You are reminded that a change in the study requires resubmission and approval of the IRB prior to initiation of the change in the study or informed consent.

It is the responsibility of the principal investigator to report to the Chair of the Institutional Review Board within 10 days, and in writing, any related unanticipated problems involving risks to subjects or others, such as adverse reactions to biological drugs, radio-isotopes or to medical devices.

Florida Hospital Institutional Review Board complies with federal and state regulations and GCP guidelines. Failure of the principal investigator or members of his/her research team to abide by the Florida Hospital IRB *Handbook for the Protection of Human Research Subjects* or failure to abide by FDA/OHRP Regulations governing this research may result in suspension and/or termination of this study.

Florida Hospital Institutional Review Board has the authority to review all documentation and the informed consent process for studies approved through the Florida Hospital IRB.

Laura Orem

Laura Orem, CIP, CIM
IRB Administrator
IRB Member
Florida Hospital IRB

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Exempt Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Sandra J. Galura**

Date: **August 10, 2010**

Dear Researcher:

On 8/10/2010, the IRB approved the following activity as human participant research that is exempt from regulation:

Type of Review:	Addendum/Modification Request Form
Modification Type:	Protocol revision to allow all surveys to be administered prior to the clinic visit if time permits; consent form revision (received 8/10/10)
Project Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Investigator:	Sandra J Galura
IRB Number:	SBE-10-06848
Funding Agency:	Sigma Theta Tau International
Grant Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Research ID:	N/A

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these changes affect the exempt status of the human research, please contact the IRB. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Joseph Bielitzki, DVM, UCF IRB Chair, this letter is signed by:

Signature applied by Janice Turchin on 08/10/2010 01:59:53 PM EDT

Janice M Turchin

IRB Coordinator

Florida Hospital
Institutional Review Board
212 E. Winter Park Street
Orlando, FL 32803
Telephone: (407) 303-5581
Fax: (407) 303-3638

March 2, 2011

Sandra Galura MSN, RN, CCRN
Nursing Research & Innovation
2312 Montano Street
Orlando FL 32803

Dear Ms. Galura:

FH #: 2453-1850; UCF Student Research
Title: Predictors of Immunosuppressant Adherence in Long-Term Renal Transplant Recipients
CPA 17249 MLM
Documents received for study continuation approval: Protocol Version 3 dated 8/10/10 and Informed consent Version 6 dated 8/10/10

Florida Hospital IRB Expedited Renewal Approval Date: 03/02/11
FH IRB Expiration Date: 02/28/12
Informed Consent/Authorization Approved: 03/02/11
Informed Consent/Authorization may not be used for subject enrollment beyond: * 02/28/12

Meeting Date for FH IRB Notification: 03/22/11

This study, which was given initial expedited approval, has been granted expedited renewal for a period of not more than one year. Unless the informed consent requirement is waived, you are required to use the IRB approved informed consent. *** Note: should the informed consent be revised, it must be approved by the IRB prior to use and will supersede the above noted approved consent/authorization.**

Prior to the expiration dated noted above, the IRB must be made aware of the status of your project(s). A progress report will be required. [21 CFR 56.109 (f)] If the project has not been completed, you may request renewed approval.

It is your responsibility to remain in compliance with all applicable state and federal regulations regarding research as well as adhering to the Florida Hospital IRB ***Handbook for the Protection of Human Research Subjects.***

You are reminded that a change in the protocol of the project requires resubmission and approval of the IRB prior to initiation of the change in protocol or informed consent.

It is the responsibility of the principal investigator to report to the Chair of the Institutional Review Board within 10 days, and in writing, any unanticipated problems involving risks to subjects or others, such as adverse reactions to biological drugs, radio-isotopes or to medical devices. Also, it is the responsibility of the principal investigator to report to the Chair of the IRB within five days, and in writing, deviations from the protocol.

Failure to abide by the Florida Hospital IRB *Handbook for the Protection of Human Research Subjects* or failure to abide by FDA/OHRP Regulations governing this research may result in suspension and/or termination of this study.

Florida Hospital Institutional Review Board has the authority to review all documentation and the informed consent process for studies approved through the Florida Hospital IRB.

Laura Orem

Laura Orem, CIP, CIM
IRB Program Manager
IRB Member
Florida Hospital IRB

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Exempt Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Sandra J. Galura**

Date: **March 10, 2011**

Dear Researcher:

On 3/10/2011, the IRB approved the following activity as human participant research that is exempt from regulation:

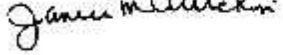
Type of Review:	Addendum/Modification Request Form
Modification Type:	Consent Form revised only to incorporate Florida Hospital stamp with new approval/expiration dates
Project Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Investigator:	Sandra J. Galura
IRB Number:	SBE-10-06848
Funding Agency:	Sigma Theta Tau International
Grant Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these changes affect the exempt status of the human research, please contact the IRB. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Joseph Bielitzki, DVM, UCF IRB Chair, this letter is signed by:

Signature applied by Janice Turchin on 03/10/2011 03:58:29 PM EST



IRB Coordinator

Florida Hospital
Institutional Review Board
212 E. Winter Park Street
Orlando, FL 32804
Telephone: (407) 303-5581
Fax: (407) 303-3638
FWA: 00002060
IRB Registration #: 00000842

DATE:	July 6, 2011
TO:	Sandra J. Galura, MSN
FROM:	Florida Hospital Institutional Review Board (IRB)
PROJECT TITLE:	[238119-3] Predictors of Immunosuppressant Adherence in Long-Term Renal Transplant Recipients
SPONSOR:	None
REFERENCE #:	2453-1850
SUBMISSION TYPE:	Other
ACTION:	APPROVED
APPROVAL DATE:	July 6, 2011
EXPIRATION DATE:	February 28, 2012
REVIEW TYPE:	Expedited Review

Note: If this is an expedited or exempt action, the full IRB will be made aware on July 26, 2011.

Thank you for your submission of Other materials for this project. The Florida Hospital IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulations. Material reviewed for this submission includes:

- Cover Sheet - IRBnetID#238119-2 Change Request Protocol Version 3 08-10-2010 (UPDATED: 07/5/2011)
- Protocol - IRBnet ID#238119-2 Protocol Version 4 07-04-2011 (UPDATED: 07/4/2011)

Please remember that informed consent is a process beginning with a description of the study and assurance of participant understanding followed by a FHIRB approved signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consent document.

Please note that any revision to previously approved materials must be approved by the FHIRB prior to initiation. Please use the appropriate revision forms for this procedure.

All UNANTICIPATED (WHICH INCLUDES SERIOUS AND UNEXPECTED) PROBLEMS involving risks to subjects or others must be reported promptly to this office. Please use the appropriate reporting forms for that submission. All FDA and sponsor reporting requirements should also be followed.

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Exempt Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Sandra J Galura**

Date: **July 05, 2011**

Dear Researcher:

On 7/5/2011, the IRB approved the following activity as human participant research that is exempt from regulation:

Type of Review:	Addendum/Modification Request Form
Modification Type:	Revision to exclusion criteria to exclude subjects enrolled on or before 07-15-2011 from participating after 07-15-2011
Project Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Investigator:	Sandra J Galura
IRB Number:	SBE-10-06848
Funding Agency:	Sigma Theta Tau International
Grant Title:	Predictors of Immunosuppressant Adherence in Long Term Renal Transplant Recipients
Research ID:	N/A

This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these changes affect the exempt status of the human research, please contact the IRB. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Kendra Dimond Campbell, MA, JD, UCF IRB Interim Chair, this letter is signed by:

Signature applied by Janice Turchin on 07/05/2011 11:44:16 AM EDT

Janice M Turchin

IRB Coordinator

APPENDIX C: CONSENTS

Sandra J. Galura MSN, RN, CCRN, CPAN
Doctoral Candidate
University of Central Florida
2312 Montana Street
Orlando, FL 32803

Predictors of Immunosuppressant Adherence in Long - Term Renal Transplant Recipients

Informed Consent

Introduction and Background: The ability to take transplant medications as prescribed is important after a kidney transplant. It is important for health care providers to know what factors help or hinder taking anti-rejection medications after kidney transplant so that they can best help patients.

Invitation to Participate: You are being invited to take part in a research study to learn about taking anti-rejection medication after kidney transplant. A total of 110 renal transplant recipients are needed for this study. The study is being conducted at Florida Hospital by Sandra Galura, MSN, RN, CCRN, CPAN, Principal Investigator, who is a doctoral student at the University of Central Florida College of Nursing.

Study Purpose: The purpose of this research is to study various factors that relate to taking anti-rejection medication after kidney transplant, and how well you take your transplant medications as they are prescribed.

Study Procedures: You are being asked to complete five short, confidential surveys on the day of your annual clinic appointment. All surveys will be administered by the principal investigator, Sandra Galura. The first survey will be given just prior to your annual clinic appointment in a room located within the Florida Hospital Transplant Clinic to gather information such as age and gender. The other four surveys will be given right after your appointment in a private room at the Clinic. These surveys will ask you about your beliefs about medicines, symptoms you experience when taking your transplant medications, support you receive from others, and the manner in which you have taken medications over the last four weeks.

Risks and Benefits of Participating: The risks associated with taking part in this study are minimal. You may be uncomfortable providing information about your symptoms or the way you take your medications. If information is discovered during this study which indicates that

Florida Hospital# 2453-1850
Patient Initials_____

Version #5 06/09/2010

you are experiencing emotional difficulties, you will be referred to the appropriate healthcare professional. There are no known benefits for your participation. Your answers may provide valuable information to healthcare providers caring for long-term renal transplant recipients.

Confidentiality of Records: You will be assigned an identifying number which will be kept on a log and linked to your name. Only the principal investigator will have access to that link. That information will be kept in the hospital in a locked file drawer that will be assigned to the principal investigator. If study results are published, your identity will remain anonymous.

Voluntary Participation: Your participation in this study is completely voluntary. You will be in this research study for one day, the day of your annual clinic appointment. It is estimated it will take one hour to complete all study surveys. There are no costs to you for participation in the study. All participants will be compensated with a $25.00 Visa gift card.

Conditions of Withdrawal: You may refuse to participate or stop participation at any time during the study without loss to benefits to which you are otherwise entitled. Should you decide not to participate or if you decide to stop participating, your relationship with your physician and the Florida Hospital Transplant Center will not be negatively affected in any way.

Your participation in the study may be stopped at any time by the principal investigator without your consent if she believes it would be in your best interest for you to stop participating.

If you have questions, concerns, or complaints about your participation in the study, contact Sandra Galura, MSN, RN, CCRN, CPAN, Principal Investigator, University of Central Florida, (407) 538-5644, Lindell Joseph, PhD, RN, Sub-Investigator, Florida Hospital Nursing Research, 407-200-2555, or Dr. Mary Lou Sole, PhD, RN, CCNS, FAAN, Faculty Supervisor, College of Nursing, University of Central Florida at 407-823-5133.

IRB contact about your rights in the study or to report a complaint: For information about the rights of people who take part in research, please contact: Florida Hospital Institutional Research Review Board, 212 E. Winter Park St., Orlando, FL 32804 or by telephone at 407-303-5581 or the Institutional Review Board, University of Central Florida, Office of Research & Commercialization, 12201 Research Parkway, Suite 501, Orlando, FL 32826-3246 or by telephone at (407) 823-2901.

Florida Hospital#__2453-1850_
Patient Initials_____

Version #5 06/09/2010

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES

The privacy laws, including the Health Insurance Portability & Accountability Act (HIPPA) and other federal and state laws, rules and regulations, protect your individually identifiable health information ("Protected Health Information"). The privacy laws require you to sign this Authorization which describes your rights and explains how your Protected Health Information will be used and disclosed for this research study entitled: **Predictors of Immunosuppressant Adherence in Long - Term Renal Transplant Recipients.**

By signing this informed consent, you are authorizing Sandra Galura MSN, RN, CCRN, CPAN, to use and disclose your Protected Health Information for the purposes described below.

Your Protected Health Information, which may be used and disclosed for this research study, includes:

- Serum creatinine level – blood test that evaluates your current kidney function.
- Serum drug levels- current levels of immunosuppressant (transplant) medications measured on the day of your annual clinic evaluation.
- Immunosuppressant medications- type of transplant medications you are taking to prevent rejection.

Your Protected Health Information will be used and disclosed by the Researchers for:

- Conducting this research study.
- Determining the ability to successfully take transplant medications as prescribed.

The Researchers may disclose your Protected Health Information to:

- The Florida Hospital's Institutional Review Board / Office
- Government representatives, when required by law.

To the extent any recipient of your Protected Health Information is not required to comply with these privacy laws, the information may no longer be protected by such privacy laws once it is disclosed to the recipient and, therefore, may be subject to re-disclosure by the recipient.

The Researchers agree to safeguard your Protected Health Information by using and disclosing it only as stated in this Authorization and as directed by state and federal law.

You will not be allowed to review your Protected Health Information that is created or obtained specifically for this research study, or treatment information that is contained in your medical record that is applicable to this research study, until after this research study is complete. When this research study is over, you will once again have the right to access this Protected Health Information.

You do not have to sign this Authorization. If you decide not to sign the Authorization:
- It will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.
- You will not be allowed to participate in this research study.

After signing the Authorization, you can change your mind and revoke this Authorization by sending a written letter to Sandra Galura MSN, RN, CCRN, CPAN, Principal Investigator, 2312 Montana Street, Orlando, FL 32803 to inform her of your decision. If you revoke this Authorization, you understand that:

- Researchers may still use and disclose the Protected Health Information **already** collected for this research study to maintain integrity of this research study.
- Your Protected Health Information may still be used and disclosed should you have an adverse event (a bad effect). If such adverse event occurs, the Researchers or Health Care Providers may need to review your entire medical record.
- You will not be allowed to continue to participate in this research study.
- You will not have access to your Protected Health Information created or obtained specifically for this research study or treatment information contained in your medical record that is applicable to this research study until the research study is complete.

This Authorization does not have an expiration date.

If you have not received a copy of the Florida Hospital Privacy Notice, please request one. If you have any questions or concerns about your privacy rights, you should contact the Florida Hospital's Privacy Officer at PH: (407) 303-9659.

This informed consent may not be used for people who do not understand the English language except with the IRB approved Short Form in the language understandable to the potential research participant.

If you agree to the terms and conditions of the study, you will consent to participate by signing below. This acknowledgement is an indication that you have read and understood the description of the study and that you agree to participate. **You will be provided with a copy of this document for your records by the principal investigator.**

Florida Hospital#__2453-1850_
Patient Initials_____

Consent:

I hereby freely and voluntarily consent to participate in the research study described in this consent. This consent is given based on written information provided, a verbal explanation of the study provided to me by the principal investigator, and the understanding that I am qualified to participate in this study.

Signature / Printed Name of Research Participant Date

I have reviewed this informed consent with the participant and have provided an explanation of the study, including that participation in this study is completely voluntary. I have answered all the participant's questions related to the study.

Signature / Printed Name of Person Obtaining Informed Consent Date

Florida Hospital#__2453-1850_
Patient Initials_____

Version #5 06/09/2010

Sandra J. Galura MSN, RN, CCRN, CPAN
Doctoral Candidate
University of Central Florida
2312 Montana Street
Orlando, FL 32803

Predictors of Immunosuppressant Adherence in Long - Term Renal Transplant Recipients

Informed Consent

Introduction and Background: The ability to take transplant medications as prescribed is important after a kidney transplant. It is important for health care providers to know what factors help or hinder taking anti-rejection medications after kidney transplant so that they can best help patients.

Invitation to Participate: You are being invited to take part in a research study to learn about taking anti-rejection medication after kidney transplant. A total of 110 renal transplant recipients are needed for this study. The study is being conducted at Florida Hospital by Sandra Galura, MSN, RN, CCRN, CPAN, Principal Investigator, who is a doctoral student at the University of Central Florida College of Nursing.

Study Purpose: The purpose of this research is to study various factors that relate to taking anti-rejection medication after kidney transplant, and how well you take your transplant medications as they are prescribed.

Study Procedures: You are being asked to complete five short, confidential surveys on the day of your annual clinic appointment. All surveys will be administered by the principal investigator, Sandra Galura. All surveys will be administered in a room located within the Florida Hospital Transplant Clinic. If time permits, all surveys will be administered prior to your clinic appointment. If time does not permit, the first survey will be given just prior to your annual clinic appointment to gather information such as age and gender. The other four surveys will be given right after your appointment in a private room at the Clinic. These surveys will ask you about your beliefs about medicines, symptoms you experience when taking your transplant medications, support you receive from others, and the manner in which you have taken medications over the last four weeks.

Risks and Benefits of Participating: The risks associated with taking part in this study are minimal. You may be uncomfortable providing information about your symptoms or the way you take your medications. If information is discovered during this study which indicates that

Florida Hospital# 2453-1850
Patient Initials_____

Version #6 08/10/2010

you are experiencing emotional difficulties, you will be referred to the appropriate healthcare professional. There are no known benefits for your participation. Your answers may provide valuable information to healthcare providers caring for long-term renal transplant recipients.

Confidentiality of Records: You will be assigned an identifying number which will be kept on a log and linked to your name. Only the principal investigator will have access to that link. That information will be kept in the hospital in a locked file drawer that will be assigned to the principal investigator. If study results are published, your identity will remain anonymous.

Voluntary Participation: Your participation in this study is completely voluntary. You will be in this research study for one day, the day of your annual clinic appointment. It is estimated it will take one hour to complete all study surveys. There are no costs to you for participation in the study. All participants will be compensated with a $25.00 Visa gift card.

Conditions of Withdrawal: You may refuse to participate or stop participation at any time during the study without loss to benefits to which you are otherwise entitled. Should you decide not to participate or if you decide to stop participating, your relationship with your physician and the Florida Hospital Transplant Center will not be negatively affected in any way.

Your participation in the study may be stopped at any time by the principal investigator without your consent if she believes it would be in your best interest for you to stop participating.

If you have questions, concerns, or complaints about your participation in the study, contact Sandra Galura, MSN, RN, CCRN, CPAN, Principal Investigator, University of Central Florida, (407) 538-5644, Lindell Joseph, PhD, RN, Sub-Investigator, Florida Hospital Nursing Research, 407-200-2555, or Dr. Mary Lou Sole, PhD, RN, CCNS, FAAN, Faculty Supervisor, College of Nursing, University of Central Florida at 407-823-5133.

IRB contact about your rights in the study or to report a complaint: For information about the rights of people who take part in research, please contact: Florida Hospital Institutional Research Review Board, 212 E. Winter Park St., Orlando, FL 32804 or by telephone at 407-303-5581 or the Institutional Review Board, University of Central Florida, Office of Research & Commercialization, 12201 Research Parkway, Suite 501, Orlando, FL 32826-3246 or by telephone at (407) 823-2901.

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Patient Initials_____

Version #6 08/10/2010

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES

The privacy laws, including the Health Insurance Portability & Accountability Act (HIPPA) and other federal and state laws, rules and regulations, protect your individually identifiable health information ("Protected Health Information"). The privacy laws require you to sign this Authorization which describes your rights and explains how your Protected Health Information will be used and disclosed for this research study entitled: **Predictors of Immunosuppressant Adherence in Long - Term Renal Transplant Recipients.**

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- Serum creatinine level – blood test that evaluates your current kidney function.
- Serum drug levels- current levels of immunosuppressant (transplant) medications measured on the day of your annual clinic evaluation.
- Immunosuppressant medications- type of transplant medications you are taking to prevent rejection.

Your Protected Health Information will be used and disclosed by the Researchers for:

- Conducting this research study.
- Determining the ability to successfully take transplant medications as prescribed.

The Researchers may disclose your Protected Health Information to:

- The Florida Hospital's Institutional Review Board / Office
- Government representatives, when required by law.

To the extent any recipient of your Protected Health Information is not required to comply with these privacy laws, the information may no longer be protected by such privacy laws once it is disclosed to the recipient and, therefore, may be subject to re-disclosure by the recipient.

The Researchers agree to safeguard your Protected Health Information by using and disclosing it only as stated in this Authorization and as directed by state and federal law.

Florida Hospital# 2453-1850
Patient Initials_____

You will not be allowed to review your Protected Health Information that is created or obtained specifically for this research study, or treatment information that is contained in your medical record that is applicable to this research study, until after this research study is complete. When this research study is over, you will once again have the right to access this Protected Health Information.

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- Researchers may still use and disclose the Protected Health Information **already** collected for this research study to maintain integrity of this research study.
- Your Protected Health Information may still be used and disclosed should you have an adverse event (a bad effect). If such adverse event occurs, the Researchers or Health Care Providers may need to review your entire medical record.
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If you have not received a copy of the Florida Hospital Privacy Notice, please request one. If you have any questions or concerns about your privacy rights, you should contact the Florida Hospital's Privacy Officer at PH: (407) 303-9659.

This informed consent may not be used for people who do not understand the English language except with the IRB approved Short Form in the language understandable to the potential research participant.

If you agree to the terms and conditions of the study, you will consent to participate by signing below. This acknowledgement is an indication that you have read and understood the description of the study and that you agree to participate. **You will be provided with a copy of this document for your records by the principal investigator.**

Florida Hospital# 2453-1850
Patient Initials_____

Consent:

I hereby freely and voluntarily consent to participate in the research study described in this consent. This consent is given based on written information provided, a verbal explanation of the study provided to me by the principal investigator, and the understanding that I am qualified to participate in this study.

Signature / Printed Name of Research Participant Date

I have reviewed this informed consent with the participant and have provided an explanation of the study, including that participation in this study is completely voluntary. I have answered all the participant's questions related to the study.

Signature / Printed Name of Person Obtaining Informed Consent Date

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Florida Hospital IRB Approved: 03/02/11
May not be used for Subject Enrollment beyond: 02/28/12
Verified by: CPA 17249

FH#: 2453-1850

Sandra J. Galura MSN, RN, CCRN, CPAN
Doctoral Candidate
University of Central Florida
2312 Montana Street
Orlando, FL 32803

Predictors of Immunosuppressant Adherence in Long - Term Renal Transplant Recipients

Informed Consent

Introduction and Background: The ability to take transplant medications as prescribed is important after a kidney transplant. It is important for health care providers to know what factors help or hinder taking anti-rejection medications after kidney transplant so that they can best help patients.

Invitation to Participate: You are being invited to take part in a research study to learn about taking anti-rejection medication after kidney transplant. A total of 110 renal transplant recipients are needed for this study. The study is being conducted at Florida Hospital by Sandra Galura, MSN, RN, CCRN, CPAN, Principal Investigator, who is a doctoral student at the University of Central Florida College of Nursing.

Study Purpose: The purpose of this research is to study various factors that relate to taking anti-rejection medication after kidney transplant, and how well you take your transplant medications as they are prescribed.

Study Procedures: You are being asked to complete five short, confidential surveys on the day of your annual clinic appointment. All surveys will be administered by the principal investigator, Sandra Galura. All surveys will be administered in a room located within the Florida Hospital Transplant Clinic. If time permits, all surveys will be administered prior to your clinic appointment. If time does not permit, the first survey will be given just prior to your annual clinic appointment to gather information such as age and gender. The other four surveys will be given right after your appointment in a private room at the Clinic. These surveys will ask you about your beliefs about medicines, symptoms you experience when taking your transplant medications, support you receive from others, and the manner in which you have taken medications over the last four weeks.

Risks and Benefits of Participating: The risks associated with taking part in this study are minimal. You may be uncomfortable providing information about your symptoms or the way you take your medications. If information is discovered during this study which indicates that

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you are experiencing emotional difficulties, you will be referred to the appropriate healthcare professional. There are no known benefits for your participation. Your answers may provide valuable information to healthcare providers caring for long-term renal transplant recipients.

Confidentiality of Records: You will be assigned an identifying number which will be kept on a log and linked to your name. Only the principal investigator will have access to that link. That information will be kept in the hospital in a locked file drawer that will be assigned to the principal investigator. If study results are published, your identity will remain anonymous.

Voluntary Participation: Your participation in this study is completely voluntary. You will be in this research study for one day, the day of your annual clinic appointment. It is estimated it will take one hour to complete all study surveys. There are no costs to you for participation in the study. All participants will be compensated with a $25.00 Visa gift card.

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- Serum creatinine level – blood test that evaluates your current kidney function.
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Florida Hospital# 2453-1850
Patient Initials_____

Consent:

I hereby freely and voluntarily consent to participate in the research study described in this consent. This consent is given based on written information provided, a verbal explanation of the study provided to me by the principal investigator, and the understanding that I am qualified to participate in this study.

DO NOT SIGN THIS CONSENT AFTER 02/28/12

Signature / Printed Name of Research Participant Date

I have reviewed this informed consent with the participant and have provided an explanation of the study, including that participation in this study is completely voluntary. I have answered all the participant's questions related to the study.

Signature / Printed Name of Person Obtaining Informed Consent Date

APPENDIX D: DATA COLLECTION TOOLS

Predictors of Immunosuppressant Adherence - Demographic

1. Predictors of Immunosuppressant Adherence - Demographic

Enter your five digit study number in the space provided. The next 8 questions will help describe the characteristics of renal tranplant patients participating in the study.

***1. Enter your five digit study identification (ID) number exactly as written on the white index card.**

***2. Enter your date of birth (mm/dd/yyyy)**

***3. What is your gender?**

- ◯ Male
- ◯ Female

***4. What is your race?**

- ◯ African American
- ◯ Asian
- ◯ American Indian / Alaska Native
- ◯ Native Hawaiian / Pacific Islander
- ◯ White

***5. What is your ethnicity?**

- ◯ Hispanic or Latino
- ◯ Not Hispanic or Latino

***6. What is your current marital status?**

- ◯ Single
- ◯ Married
- ◯ Living together
- ◯ Separated / Divorced
- ◯ Widowed

Predictors of Immunosuppressant Adherence - Demographic

***7. What is your current employment status?**

- ◯ Full time (36-40 hours per week)
- ◯ Part time (<36 hours per week)
- ◯ Not currently employed

***8. What is the highest level of education you have completed?**

- ◯ Grammar school
- ◯ High school or equivalent
- ◯ Vocational / technical school (2 year)
- ◯ Some college
- ◯ Bachelor's degree
- ◯ Master's degree
- ◯ Doctoral degree

9. Annual Income

- ◯ < $10,000
- ◯ $10,000 - $29,999
- ◯ $30,000 - $59,999
- ◯ $60,000 - $99,999
- ◯ $100,000 -$249,999
- ◯ > $250,000

Predictors of Immunosuppressant Adherence - Demographic Investigator

1. Predictors of Immunosuppressant Adherence - Demographic Investigator Collec...

***1. Five digit study identification number.**

***2. Date of initial transplant (mm/yyyy).**

***3. Enter participant immunosuppressant medications**

	Dose	Frequency
Arava		
Azathioprine (Imuran)		
mycophenolate mofetil (CellCept)		
mycophenolate sodium (Myfortic)		
tacrolimus (Prograf)		
Sirolimus (Rapamune)		
Prednisone		

***4. Number of immunosuppressant medications (types) in regimen.**

***5. Number of pills per day in regimen**

***6. Number of times patient takes medications per day.**

7. tacrolimus (Prograf) - target after 3 months (6-8 ng/ml)

8. tacrolimus assay

9. sirolimus (Rapamune) assay - target 8-15 ng / ml

10. sirolimus assay

***11. Serum creatinine level (0.6-1.2 mg / dL).**

Predictors of Immunosuppressant Adherence - Demographic Investigator

***12. If serum creatinine outside normal range, is value within patient's maintenance baseline?**

- ◯ Yes
- ◯ No
- ◯ Not applicable: value within normal range

13. Reference lab.

- ◯ Florida Hospital
- ◯ Outside lab (other)

Outside lab normal values

***14. Primary insurance provider.**

- ☐ Medicare
- ☐ Medicaid
- ☐ Private insurance
- ☐ No insurance - self pay

Beliefs About Medicines Questionnaire (BMQ)

1. Beliefs About Medicines Questionnaire

Enter your five digit study number in the space provided. The next 10 questions are statements that other people have made about medications prescribed for them. You are being asked to rate your level of agreement with questions about the immunosuppressant medications prescribed for you. You are to rate your response to the question from strongly disagree (1) to strongly agree (5).

***1. Please enter your five digit study number**

***2. My health, at present, depends on my medicines.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***3. My life would be impossible withtout my medicines.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***4. Without my medicines I would be very ill.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***5. My health in the future will depend upon my medicines.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***6. My medicines protect me from becoming worse.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***7. Having to take medicines worries me.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***8. I sometimes worry about long-term effects of my medicine.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***9. My medicines are a mystery to me.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***10. My medicines disrupt my life.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

***11. I sometimes worry about becoming too dependent on medicines.**

◯ Strongly disagree ◯ Disagree ◯ Uncertain ◯ Agree ◯ Strongly agree

MOS Modified Social Support Survey (MSSS)

1. MOS Modified Social Support Survey (MSSS)

Enter your five digit study number in the space provided. People sometimes look to others for companionship, assistance, or other types of support. The next 18 questions cover the types of support that would be available to you if you needed it. Please select the appropriate response (none of the time, a little of the time, some of the time, most of the time, or all of the time) based on the support available to you in the last 4 weeks.

***1. Enter your five digit study identification (ID) number exactly as written on the white index card.**

***2. How often is someone available to help if you are confined to a bed?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***3. How often is someone available to listen to you when you need to talk?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***4. How often is someone available to give you good advice about a crisis?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***5. How often is someone available to take you to the doctor if you need to go?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***6. How often is someone available to show you love and affection?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***7. How often is someone available to have a good time with?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***8. How often is someone available to give you information to help you understand a situation?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***9. How often is someone available to confide or talk to about yourself or your problems?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

***10. How often is someone available to hug you?**

◯ None of the time ◯ A little of the time ◯ Some of the time ◯ Most of the time ◯ All of the time

MOS Modified Social Support Survey (MSSS)

***11. How often is someone available to get together with for relaxation?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***12. How often is someone available to prepare your meals if you are unable to do so?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***13. How often is someone available whose advice you really want?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***14. How often is someone available to help with daily chores if you are sick?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***15. How often is someone available to share your private worries and fears with?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***16. How often is someone available to turn to for suggestions about how to deal with a personal problem?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***17. How often is someone available to do something enjoyable with?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***18. How often is someone available to understand your problems?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

***19. How often is someone available to love and make you feel wanted?**

○ None of the time ○ A little of the time ○ Some of the time ○ Most of the time ○ All of the time

Basel Assessment of Adherence with Immunosuppressive Medications

1. The Basel Assessment of Adherence with Immunosuppressive Medications Scale ...

Enter your five digit study number in the space provided. Taking immunosuppressive medications after transplantation can be difficult for many patients. The next 9 questions will explore with you how you manage medications in daily life.

***1. Enter your five digit study identification (ID) number exactly as written on the white index card.**

***2. Do you recall not having taken your immunosuppressive medications some times in the past 4 weeks?**

◯ Yes ◯ No

***3. Could you tell me how often this happened?**

◯ Never ◯ Once per month ◯ Every two weeks ◯ Every week ◯ More than once a week ◯ Every day

***4. Have you skipped several consecutive doses of your immunosuppresive medications in the past 4 weeks?**

◯ Yes ◯ No

***5. Could you tell me how often this happened?**

◯ Never ◯ Once per month ◯ Every two weeks ◯ Every week ◯ More than once per week ◯ Every day

***6. Do you recall having taken your immunosuppressive medications with more than 2 hours time difference from the prescribed dosing time in the past 4 weeks?**

◯ Yes ◯ No

***7. Could you tell me how often this happened?**

◯ Never ◯ Once a month ◯ Every two weeks ◯ Every week ◯ More than once per week ◯ Every day

***8. Have you reduced the prescribed amount of your immunosuppressive medications during the past 4 weeks?**

◯ Yes ◯ No

Page 1

Basel Assessment of Adherence with Immunosuppressive Medications

***9. Could you tell me how often this happened?**

◯ Never ◯ Once per month ◯ Every two weeks ◯ Every week ◯ More than once per week ◯ Every day

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

1. Modified Transplant Symptom Occurrence and Symptom Distress Scale (MTSOSD- ...

Enter your five digit study number in the space provided.

Taking your medications after transplantation is associated with certain side effects, which may or may not be distressing to you. You will be asked two questions each about 59 symptoms associated with transplant medications.

The first question will ask you to indicate how frequently or how often you have experienced a given symptom during the past four weeks (never, occasionally,regularly, almost always, always). If the symptom does not occur, answer "never".

The second question will ask you if these symptoms are distressing to you (0-not distressing to 4-terribly distressing). If you do not have the symptom, then you answer "N/A".

1. Enter your five digit study number.

***2. I have had itching.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***3. My itching was:**

	0- Not distressing	1	2	3	4- Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***4. I have had chest pain.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***5. My chest pain was:**

	0-Not distressing at all	1	2	3	4- Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***6. I have had wind.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***7. My wind was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***8. I have had increased thirst.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***9. My increased thirst was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***10. I have felt restless or nervous.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***11. My restlessness or nervousness was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***12. I have had hearing loss.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***13. My hearing loss was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***14. I have had abnormal skin color.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***15. My abnormal skin color was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***16. I have had increased sweating.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***17. My increased sweating was:**

	0- Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***18. My face and neck have been red.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***19. The redness in my face and neck was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***20. I have had brittle fingernails.**

○ Not ○ A little ○ Moderately ○ Greatly ○ Very greatly

***21. My brittle fingernails were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	○	○	○	○	○	○

***22. My breasts have been larger.**

○ Not ○ A little ○ Moderately ○ Greatly ○ Very greatly

***23. My breast enlargement was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	○	○	○	○	○	○

***24. I have had sores on my lips and/or in my mouth.**

○ Never ○ Occasionally ○ Regularly ○ Almost always ○ Always

***25. My sores on lips and /or in mouth were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	○	○	○	○	○	○

***26. I have had an altered voice.**

○ Not ○ A little ○ Moderately ○ Greatly ○ Very greatly

***27. My altered voice was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	○	○	○	○	○	○

***28. I have had oily skin.**

○ Never ○ Occasionally ○ Regularly ○ Almost always ○ Always

***29. My oily skin was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	○	○	○	○	○	○

***30. I have felt dizzy.**

○ Never ○ Occasionally ○ Regularly ○ Almost always ○ Always

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***31. My dizziness was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***32. My hands have trembled.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***33. My trembling hands were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***34. I have had an increased urge to urinate.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***35. My increased urge to urinate was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***36. I have had a feeling of warmth in my hands and feet.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***37. The feeling of warmth in my hands and feet was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***38. I have had bruises more easily.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***39. My bruises were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***40. I have had sores or warts around my genitals.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***41. My sores or warts around genitals were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***42. I have had spots on my face and/or my back.**

Never | Occasionally | Regularly | Almost always | Always

***43. My spots on my face and/or back were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing						

***44. I have had an excessive appetite.**

Never | Occasionally | Regularly | Almost always | Always

***45. My excessive appetite was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing						

***46. I have felt depressed.**

Never | Occasionally | Regularly | Almost always | Always

47. My feelings of depression were:

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing						

***48. My gums have swollen.**

Not | A little | Moderately | Greatly | Very greatly

***49. My swollen gums were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing						

***50. I have had swolleen glands in my neck, armpit, or groin.**

Never | Occasionally | Regularly | Almost always | Always

51. My swollen glands were:

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing						

***52. I have had thinning of hair or hair loss.**

Not | A little | Moderately | Greatly | Very greatly

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***53. My hair thinning or hair loss was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***54. I have had menstrual problems (females only).**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly ◯ N/A

55. My menstrual problems were (females only):

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***56. I have had erectile problems (for males only)**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always ◯ N/A

***57. My erectile problems were (for males only):**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***58. I have had a puffy face (moon face).**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***59. My puffy face was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***60. I have had swollen ankles or feet.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***61. My swollen ankles or feet were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***62. I have had diarrhea.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***63. My diarrhea was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***64. I have had tingling or numbness in my hands or feet.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***65. My tingling or numbness in my hands or feet was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***66. I have had back pain.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***67. My back pain was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***68. I have had a brittle skin.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***69. My brittle skin was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***70. I have felt anxious.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***71. My feelings of anxiety were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***72. I have been experiencing mood swings.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***73. My mood swings were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***74. I have had headaches.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***75. My headaches were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***76. My facial features have changed.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***77. My changed facial features were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***78. I have had fat deposits on my neck and back (buffalo hump).**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***79. My fat deposits on neck and back were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***80. I have had difficulty concentrating and/or memory problems.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***81. My concentration difficulties and/or memory problems were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***82. I have had warts on hands and feet.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***83. My warts on hands and feet were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***84. I have had increased hair growth on my face and body.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***85. My increased hair growth on face and body were:**

	0-Not terribly distressing	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***86. I have had sleep difficulties.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***87. My sleep difficulties were:**

	0-Not terribly distressing	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***88. I have had muscle weakness.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***89. My muscle weakness was:**

	0-Not terribly distressing	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***90. My sense of taste has changed.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***91. The change in my sense of taste was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***92. I have had a poor apetite.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***93. My poor appetite was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***94. I have felt tired.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***95. My tiredness was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distrssing	◯	◯	◯	◯	◯	◯

***96. I have had a lack of energy.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***97. My lack of energy was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***98. I have had stomach complaints, I have felt nauseous and/or I had to vomit.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***99. My stomach complaints, nausea or vomiting were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***100. I have had pain in my joints.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***101. My joint pain was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***102. I have had a rash on my skin.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***103. My skin rash was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***104. I have had muscle cramps.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***105. My muscle cramps were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***106. I have had nightmares.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***107. My nightmares were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***108. I have been short of breath.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***109. My shortness of breath was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***110. I have had a dry skin.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***111. My dry skin was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***112. I have had palpitations.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***113. My palpitations were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***114. I have had constiptation.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***115. My constipation was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***116. I have had difficulty seeing well.**

◯ Not ◯ A little ◯ Moderately ◯ Greatly ◯ Very greatly

***117. My seeing difficulties were:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***118. I have had a reduced interest in sex.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

Modified Transplant Symptom Occurrence and Symptom Distress Scale -

***119. My reduced interest in sex was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

***120. My eyes have been sensitive to light.**

◯ Never ◯ Occasionally ◯ Regularly ◯ Almost always ◯ Always

***121. My sensitivity to light was:**

	0-Not distressing at all	1	2	3	4-Terribly distressing	N/A
Distressing	◯	◯	◯	◯	◯	◯

122. I have also been experiencing the following side effect:

123. I have experienced this side effect:

	Never	Occasionally	Regularly	Almost Always	Always
Frequency	◯	◯	◯	◯	◯

124. This side effect was:

	0-Not distressing at all	1	2	3	4- Terribly distressing
Distressing	◯	◯	◯	◯	◯

125. I have also been experiencing this side effect:

126. I have experienced this side effect:

	Never	Occasionally	Regularly	Almost Always	Always
Frequency	◯	◯	◯	◯	◯

127. This side effect was:

	0-Not distressing at all	1	2	3	4-Terribly distressing
Distressing	◯	◯	◯	◯	◯

128. I have also been experiencing the following side effect:

129. I have experienced this side effect:

	Never	Occasionally	Regularly	Almost Always	Always
Frequency	◯	◯	◯	◯	◯

130. This side effect was:

	0-Not distressing at all	1	2	3	4-Terribly distressing
Distressing	◯	◯	◯	◯	◯

Clinician Collateral Report of Adherence

1. Default Section

***1. Five digit study identification number.**

***2. I rate this study participant's overall level of immunosuppressant medication adherence as:**

- ◯ Good: No clinical evidence of nonadherence; no patient self-report of nonadherence.
- ◯ Fair: Either clinical evidence of nonadherence or patient self-report of nonadherence.
- ◯ Poor: Both clinical evidence of nonadherence or patient self-report of nonadherence.
- ◯ Missing Data Point

***3. Practitioner type:**

- ◯ Physician Provider
- ◯ Nurse Practitioner
- ◯ Transplant Clinic Nurse
- ◯ Missing Data Point

APPENDIX E: LETTERS GRANTING PERMISSION

From: sandragalura <sandragalura@knights.ucf.edu>
To: sgalura <sgalura@aol.com>
Subject: FW: Doctoral Candidate Dissertation Request - BAASIS Instrument / MTSOSD-59R
Date: Sat, 6 Feb 2010 7:11 pm
Attachments: MTSOSD-m&f-oriq_mapi.pdf (55K), 2008_EXPLANATION__MTSOSD-R59.pdf (56K), BAASIS_2009_English.pdf (29K), BAASIS_2009_explanation.pdf (61K)

> Date: Fri, 25 Dec 2009 19:34:11 +0100
> From: sabina.degeest@unibas.ch
> To: sandragalura@knights.ucf.edu
> Subject: Re: Doctoral Candidate Dissertation Request - BAASIS Instrument / MTSOSD-59R
>
> Dear Mrs Galura
> Thank you for your mail
> Please find attached the MTSOSD-R59 as well as an explanation of the
> scale. The scale is under copyright and can only be used for free in
> academic independent research
> Concerning the BAASIS, I can inform you that we are currently revising
> this instrument based on the experiences of previous studies. I attach
> the 2009 version and explanation of the scale. The 2010 version will be
> released the beginning of the year. The scale is under copyright and can
> only be used for free in academic independent research
> In case you would be interested in using this scale please inform me and
> we can forward the new version in a few weeks to you
> We would appreciate a short outline of your research for our files as
> well as your details
> I wish you all success with your research
> With kind regards
> Sabina
>
> sandragalura@knights.ucf.edu wrote:
> > Dear Dr. De Geest,
> >
> > I am currently enrolled doctoral candidate with the College of Nursing
> > at the University of Central Florida in Orlando Florida. My
> > dissertation is focused on exploring predictors of IST adherence in
> > renal transplant recipients surviving long term (> 4 years). I have
> > had the priviledge of following your lengthly work regarding
> > adherence during my course work over the past four years as I have
> > learned of the issues facing renal transplant recipients.
> >
> > I recently contacted you respectfully requesting a copy of the updated
> > MTSOSD-59R Modified Transplant Symptom Occurrence and Distress Scale.
> > While I am still very interested in obtaining a copy of this tool
> > pending your approval, I also have a few questions regarding a
> > recently published study entitled /Nonadherence to Immunosuppressive
> > Medication in Renal Transplant Recipients within the Scope of the
> > Integrative Model of Behavioral Prediction (2009). /In that study,

FLORIDA HOSPITAL
Transplant Center

www.fhtransplant.com

January 21, 2010

RE: Research Approval for Sandra Galura

To Whom It May Concern:

On Wednesday, January 21, 2010, I met with Sandra Galura to discuss her dissertation and research proposal. Sandra is granted approval to conduct the study within the Florida Hospital Transplant Center pending IRB approval and approved informed consent.

If you require any further information, please contact me at 407.303.3628.

Sincerely,

Cyndi J. Bergs, MBA, MHA
Assistant Director
Florida Hospital Transplant Center

Transforming
Lives for More
Than 30 Years

2501 N. Orange Avenue • South Tower, Suite 514 • Orlando, FL 32804 • Tel: 407.303.2474 • Fax: 407.303.2478

Galura, Sandra

From: Burgess, Leigh Ann
Sent: Wednesday, March 03, 2010 1:27 PM
To: Galura, Sandra
Cc: Bergs, Cynthia
Subject: RE: Doctoral Dissertation Research Request

Sandra,
I apologize for my delay… I approve.
Thanks

From: Galura, Sandra
Sent: Sunday, February 28, 2010 8:36 PM
To: Burgess, Leigh Ann
Cc: Bergs, Cynthia
Subject: RE: Doctoral Dissertation Research Request

Dear Leigh Ann,

I was following up to see if you had time to consider my below request? I have already met with Cynthia Bergs to discuss my research project, but need to secure your approval to obtain a research project number and begin the IRB process at Florida Hospital.

I will be happy to meet with you at your convenience to further clarify my project.

Thank you.

Sincerely,

Sandra Galura MSN, RN, CCRN, CPAN
Clinical Nurse Educator
Post Anesthesia Care Unit
Florida Hospital Orlando
sandra.galura@flhosp.org
Telephone 407-303-1961
Beeper 8431
Spectra-Link 110-6536

From: Galura, Sandra
Sent: Fri 2/19/2010 7:58 AM
To: Burgess, Leigh Ann
Cc: Bergs, Cynthia
Subject: Doctoral Dissertation Research Request

Dear Lee Ann,

My name is Sandra Galura. Approximately one year ago I spent an academic semester in your transplant clinic completing an independent study for my doctoral program. Since then, I have completed course work, candidacy,

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