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The Utility of Independent and Interrelated Parent and Child Reports
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Chapter I: Review of the Literature

Fifty-years ago a child diagnosed with end-stage-renal-disease (ESRD) would have had no chance of survival. Since that time, medical advancements have greatly improved the likelihood of long-term survival. Children who now receive the diagnosis of ESRD have a good chance of living into their late adult years. Increased life expectancy in patients with ESRD is due primarily to the innovation and continual advancements of immunosuppressant medications, which allow for kidney transplantation (Rodrigue & Sobel, 2003). However, as medical advancements increase survival, they also present new challenges for patients, families, and clinicians.

Transplantation as a treatment for ESRD began with the first kidney transplant in a human being in the 1950s, between a set of identical twin girls. Shortly after, in the 1960s, advancement in medications allowed patients to receive a kidney from a non-related donor without rejection. In the decades that followed, transplantation became more common as a treatment for ESRD. By the late 1980s, immunosuppressant medications were advancing, which decreased rejection and increased the amount of graft survival (Hatch & Agrawal, 2009).

Prior to further examination on the topic of renal transplantation, it would be beneficial to define a few key words. “Graft” is the tissue that is transplanted into part of the body in order to repair or replace something that is defective. In the instance of kidney transplantation, the graft is the new kidney that is put into the body, which is also
known as the “host”. Rejection of the organ occurs when the graft that is put into the host is destroyed by the host’s immune system. Rejection can happen in one of two ways: chronically or acutely. Chronic rejection is an ongoing destruction of the transplanted organ and typically occurs awhile after transplantation. Acute rejection, on the other hand, occurs shortly after transplantation and is when the host body destroys the new organ (Venes, 2005). Both types of rejection are combated primarily by the use of regular immunosuppressant medications. Therefore, not taking medications consistently will increase the likelihood of both types of rejection.

Increase in survival since the first kidney transplant is due to a variety of factors besides the advancement in immunosuppressant medications (Seikaly, Ho, Emmett, & Tejani, 2001). First, it has been found that kidneys from cadaver donors are more likely to be rejected after one year than living-donor kidneys. There has been an increase since 1987 in kidney transplants coming from living donors. Two proposed reasons for better clinical outcomes include: shorter or no time spent on dialysis and a better HLA match between the donor and recipient (Hardy, Shah, Cicciarelli, Lemley, Hutchinson, & Cho, 2009). Second, the changes in disease patterns and rates of progression of ESRD have decreased the number of children needing to receive a transplant. Infants and children have been found to have lower rates of graft survival within the first year. However, once the graft survives the first year, infants and children have a reduced rate of graft loss in later years when compared to adolescents and adults without taking into consideration the age that the individual had the transplant (Cecka, Gjertson, & Terasaki, 1997). Finally, there has been an increase in recognition of initial signs of rejection. This allows more
people to avoid complete rejection, and, therefore, the need for an additional kidney transplant.

Each year, an average of 5,700 children and adolescents under the age of 18 have the diagnosis of ESRD (Government Accountability Office, GAO, 2007). The options for treatment include: peritoneal dialysis, hemodialysis, and renal transplantation (Hatch & Agrawal, 2009). Approximately two-thirds of children with ESRD will have a successful transplant and one-third will receive dialysis treatment (Government Accountability Office, GAO, 2007). Most often kidney transplantation is the preferred method of treatment. Transplantation, compared to life-long dialysis, has been found to increase quality of life, as well as decrease long-term mortality rates (Horslen, Barr, Christensen, Ettenger & Magee, 2007).

Although clinical outcomes have improved in all age groups, there are differences in outcomes of children compared to adolescents. One-year post transplant, children under the age of 11 have more graft loss than that of adolescents. However, as patients get further from transplant, clinical outcomes for each age group change. Regardless of age at time of transplant, adolescents have been found to have more graft loss than children five-years post transplant (Dobbels, Van Damme-Lombaert, Vanhaecke, & De Geest, 2005). The variability in clinical outcomes has several proposed reasons, but authors primarily point to non-adherence, which is found to be higher in adolescents than in children (Dobbels et al., 2005; Smith, Ho, & McDonald, 2002).

**Renal Transplantation Treatment Regimen**

After undergoing renal transplantation there are many components involved in the treatment regimen. Three areas of primary significance are: attending clinic visits,
completing lab work, and taking oral medications. In the months following transplantation, children have multiple clinic visits every week. In addition, they have labs drawn equally as frequently in order to monitor kidney functioning and regulate medication. The frequencies of both clinic and lab visits decrease as the child gets further from transplant; however, they remain important parts of the treatment process for the remainder of the child’s life. The final significant component to the treatment regimen is taking oral medication. This can consist of a large number of medications when the child leaves the hospital. Taking oral medications is particularly difficult for children who have undergone renal transplantation due to the fact that different medications are given at different times throughout the day and they have a variety of different side effects. In order to prevent rejection, all of the children are on some form of immunosuppressant medication for the remainder of their lives. In addition to taking immunosuppressant medications, labs are conducted to determine the absorption of the current dosage of medication in order to assure it is an effective dose, while preventing toxicity. Medication dosages are changed by the physician based on the results. Directly following transplant labs can be done, and therefore medication dosages can be changed, as often as multiple times per week. There is the expectation that families will understand the changes and will be able to keep up with this ever-changing regimen (Hricik, 2003).

Despite the difficulty in maintaining the immunosuppressant medication regimen, it is of utmost importance to do so correctly. When a kidney is transplanted, the host body recognizes the new organ as a foreign object. The host’s immune system starts to fight off the new kidney. Immunosuppressant medications weaken the host’s immune system in order to prevent it from destroying the new organ. Medications are constantly being
altered in order to best protect the transplanted kidney, while still allowing the host to have as effective of an immune system as possible in order to prevent future illness and infection. While rejection can occur when the patient is properly taking his or her immunosuppressant medications, the risk of rejection significantly increases when the patient fails to strictly adhere to the medication regimen (Roche Laboratories, 1997).

**Overview of Adherence**

Traditionally, adherence is defined as “the extent to which a person’s behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice” (Haynes, Taylor, & Sackett, 1979). Advances in medicine continue to be achieved, however, they can only be beneficial to the extent in which individuals use them properly.

Before discussing specific research in the area of adherence, it is first necessary to understand the way in which research in this field is conducted. Researchers face several inherent difficulties. The two primary topics to consider are: definition of adherence and method used to measure adherence. It is important to remember when comparing studies that they all use the term ‘adherence,’ but they may be using different definitions and measurements of adherence.

While the formal definition of adherence is not generally debated, researchers widely vary in the operational definition of the term. For example, some may choose to define being adherent as not missing a single dose over a period of a week or a month. Others may calculate a percentage of how many doses the person took out of the total number prescribed (Quittner, Modi, Lemanek, levers-Landis, & Rapoff, 2007). Commonly, studies using a dichotomous (adherent verses not adherent) approach
consider patients to be adherent if they take 80% of their prescribed medication (Cramer, 2009). Not only does research vary in the way that adherence is defined, but also in the way that criteria that contribute to the definition are measured. Each method of measurement has advantages and disadvantages.

Ways of measuring adherence include self-report, pharmacy refill histories, daily-diaries, and biological assays. Self-report is the most commonly used measure of adherence (Quittner et al., 2007). Data can be gathered quickly and inexpensively which can allow for a large sample size. Despite its popularity, it has been found that self-report data consistently overestimates the level of adherence when compared to other methods of adherence. This is hypothesized to be due partially to an individual's inaccurate perception of his or her adherence, as well as to social desirability. Both inaccurate perceptions and social desirability are disadvantages of all types of self-reported data. Pharmacy refill histories are difficult to assess due to the fact that histories are collected through pharmaceutical databases, which are not yet standardized. The daily-diary method can be used in many different forms, including: written logs, time-sensitive reminders, or regular phone calls from the researcher to report adherence. Yet, daily-diaries have been found to be more accurate than other kinds of self-report measures but still have many of the same social desirability biases. Again, this can lead to an inflated rate of reported adherence (Quittner et al., 2007). Another method is drug assays. A drug assay is a measurement of the amount of medication in the body at the time of the blood draw. Drug assays are specific to the medication that is being prescribed to the patient, which is determined based on the disease that is being treated. Some diseases have more validated drug assay values than others. This is an objective way to measure adherence,
however, it does have disadvantages. Primarily, most drug assays only capture the amount of the drug present in the body directly preceding the blood draw. Therefore, adherence is being determined based on only a few days of the child’s life. In addition, drug assay results may be indicating the body’s metabolism of the drug, rather than medication adherence. Low levels of the drug may be assumed to be a lack of adherence, when in fact, the person’s body is not responding to the drug in the way that is expected (Vitolins, Rand, Rapp, Ribisl, & Sevick, 2000). All of these methods are commonly used in adherence research.

There is one additional method of measuring adherence that currently is considered to be the “gold standard” of measuring adherence is electronic monitoring (Quittner et al., 2007). Electronic monitors are devices given to the patient for some period of time that record the time of day that the dose is taken. The specific monitors widely vary based on the disease population being studied. For example, there are devices that are similar to pill bottles for research that is studying adherence to oral medication; while a device that fits on inhalers for research is used to study adherence in the population with asthma. The different devices collect the data, which researchers download to get a fairly reliable measure of real-time adherence. However, despite the progress that is being made with electronic monitors, they still have many potential disadvantages. First, as with all technology, they have the potential to malfunction. Data can be lost or recorded incorrectly if the monitor is not working properly and then assumed to be an accurate representation of the participant’s adherence. The monitor can be lost or simply not returned by the participant, again resulting in missing data. Another disadvantage is the high cost of these devices. For example, a MEMS cap, which is a
popular method of measuring adherence, costs approximately $130 (Quittner et al., 2007). This makes them expensive to use in research and very difficult to consider using in a clinical setting. Some research has found that participants dislike using electronic monitoring devices and find them harmful to the adherence process. This can lead to a biased group of participants willing to partake in the study, as well as misleading results (Shellmer & Zelikovsky, 2007). A final, and serious, concern is that there are certain assumptions that are being made with the monitors. For example, the medication event monitoring system (MEMS) cap records the time that the bottle is opened. It is assumed that the patient is removing and ingesting those medications from the bottle and taking only the prescribed dose. While they have disadvantages, electronic monitors are the only method currently available with the advantage of having a real-time collection of data. However, due to the fact that electronic monitors are not perfect measures of adherence, it is still ideal to be able to use multiple methods of measuring adherence (Quittner et al., 2007). Due to limitations in research, such as limited sample size, it is not always feasible to use multiple methods. These limitations, along with the fact that there is not a well-established way of combining adherence measures, often force researchers to choose only one method of measuring adherence. Based on current research, electronic monitoring is the most accepted, single way of measuring adherence.

**Consequences of Nonadherence**

There are a number of potential negative consequences when patients do not adhere to their medication regimens. In chronically ill patients as a group, consequences of nonadherence include, but are not limited to: poorer health and the decreased well-being for the patient, up to and including death, increased cost of medical care, incorrect
clinical decisions, and inaccurate conclusions in research (Rapoff, 1999). The health impact of nonadherence varies widely based on the population being studied. The consequences can include a variety of symptoms with varying levels of severity depending on the disease. In addition, nonadherence can lead to an increased number of visits to the emergency room and inpatient hospital stays. These are all consequences that affect the well-being of the patient, as well as the cost of medical care.

Higher medical cost is one area that Rapoff (1999) identified as a consequence of nonadherence in chronic illness populations in general. The significance of adherence is made evident when considering that over $300 billion is estimated to be spent annually in the United States due to issues related to nonadherence for all diseases combined (Bender & Rand, 2004). This cost affects both taxpayers and the families who already have large medical expenses (Rapoff, 1999). These expenses might be avoidable if the issue of adherence is more widely addressed. It should be addressed both in the literature, as well as in the clinical setting, as adherence should be a concern not only for patients, but also for health-care providers (Berlant & Pruitt, 2003).

According to Rapoff (1999), two additional areas that nonadherence impacts are incorrect clinical decisions and false results of clinical trials. Decisions, such as medication dosages, are often made in the clinic in order to best treat the patient’s disease. However, decisions are made based on self-reported adherence by patients despite the fact that patients have been found to overestimate their level of adherence. Therefore, decisions are made that could be less effective or even harmful to the patient because the physician may not be getting an accurate picture of how well the current regimen is working. On a more global level, research is constantly being done on
medication regimens to improve treatment for children in different illness populations. If current patients are not fully adhering to their regimens, a distorted understanding of the medication’s effectiveness is being formed. This misrepresentation of the usefulness of a given medication can be dangerous for current patients, as well as future patients who will be undergoing the same medication regimens.

Despite the fact that these are known consequences of nonadherence, adherence remains a large problem in children with chronic illnesses. While research varies on the rates of nonadherence, it is estimated that 50% of children who have a chronic illness are not adherent to their regimen. The numbers for adolescents with chronic illnesses are thought to be even worse, with a nonadherence rate estimated to be closer to 65-75% (Rapoff & Barnard, 1991). Additionally, within the chronic illness population, research suggests that nonadherence may be even more common than reports currently indicate due to the difficulty of obtaining adherence information (Rapoff, 1999).

**Examples of Adherence Research in Specific Populations**

While overall rates of adherence in pediatric chronic illnesses are reported in summary chapters and in meta-analyses, research in the area of adherence is typically done with specific populations. Children who are HIV positive constitute one disease population that heavily relies on constant and regular medication intake. A thorough review of the literature regarding adherence in children who are HIV positive found results that are fairly consistent with overall estimates of adherence in children with chronic illnesses in general. This particular illness is understudied and methods of measuring adherence widely vary. Therefore, the authors were not able to form conclusive results, however, they estimated that rates of nonadherence were between 25
and 50% (Steele & Grauer, 2003). In this population, nonadherence is dangerous due to the fact that resistant antiviral strains are more likely to develop when medication is not consistently present in the body to fight off the antiviral strains that are already present. Despite the fact that there are serious, long-term consequences of not taking medication, adherence rates appear to be similar, or only slightly higher, than rates in children with chronic illnesses in general.

Each chronic illness has a different treatment regimen. For instance, in diabetes, the regimen does not typically involve taking oral medications, however, there are numerous other components. These include checking blood sugars, injecting insulin, changing diet habits, and attending regular clinic appointments. Since diabetes is an illness that affects over 186,000 children and adolescents (National Diabetes Education Program, 2008) more research is done with this population. Not only does diabetes affect more children, but, there is also the advantage of obtaining larger sample sizes and, therefore, having the ability to obtain more conclusive results (Wysocki, Greco, & Buckloh, 2003). A recent meta-analysis reviewed the literature with the aim of solidifying the relationship between adherence and glycemic control in youth. Hood, Peterson, Rohan, and Drotar (2009) reviewed 21 studies, with a total of 2,492 participants with Type 1 diabetes mellitus. The authors concluded through their examination of past research that the connection between adherence and glycemic control is, in fact, strongly related. As adherence increased, HgA1c levels decreased, indicating improved glycemic control. Research regarding adherence in Type 1 diabetes is important for the large body of literature and quality of studies.

Similar advantages exist within the asthma population. The prevalence of asthma
has dramatically increased over the past several decades (Akinbami, 2006), so large scale studies are more common. One study compared electronic monitoring of adherence with parent and child self-report. Self-report of adherence was approximately 80%. In contrast, electronic monitoring showed adherence rates to be closer to 69%. Furthermore, monitors typically have the ability to allow for more than 100% adherence on a given day, which can inflate the overall percentage of adherence. When the monitors were set to allow a maximum of 100% adherence on a given day, rates of adherence were only 50% (Bender et al., 2000). These results indicate that rates of adherence appear to be similar in the asthma population as compared to other chronic illness populations. It also points to the significance of the way that adherence is measured. This is an overarching problem in adherence research.

A final study examining the degree of adherence in adolescents who have undergone a liver transplant found results similar to those of the previously discussed populations. A study by Fredericks, Magee, Opipari-Arrigan, Shieck, Well, and Lopez (2008) used three different methods of measuring adherence: drug assays, self-report, and rates of clinic attendance. The authors concluded that each method of measurement was capturing a different aspect of adherence. This conclusion was due to the fact that the results from each method did not correlate with either of the other methods. However, when combining these methods, 76% of the adolescents were found to be nonadherent by at least one measure. As seen with other illnesses, this finding indicates poor rates of adherence in a condition that relies heavily on consistent oral medication intake, and has a fairly similar regimen to that of the renal transplant population.
Adherence in the Renal Transplant Population

As with chronic illnesses in general, one reason adherence is important to address in patients who have undergone renal transplantation is the cost associated with nonadherence (Pinsky, Takemoto, Lentine, Burroughs, Schnitzler, & Slavalaggio, 2009). On average, the annual cost for a child who has a successful renal transplant is $4,916 post-transplant. However, a child with kidney failure following a transplant has an average annual cost of $41,929 (Government Accountability Office, GAO, 2007). This number includes patients who have failure due to reasons other than nonadherence; however, nonadherence is a leading cause of kidney failure following a transplant (Butler, Peveler, Roderick, Horne, & Mason, 2003).

Beyond the cost associated with nonadherence, there are several clinically important reasons for a child to be adherent to his or her medical regimen. While a kidney transplant may resolve ESRD, the recipient is faced with a new set of medical challenges. The lifetime requirements of immunosuppressant medication and repeated, and sometimes frequent, demands of lab testing and medical appointments create a situation akin to having a chronic illness. Research involving children with ESRD has shown rates of nonadherence that widely vary. A meta-analysis done with pediatric renal transplant recipients found rates of nonadherence to range from 5% to over 75% (Dobbels et al., 2005). A recent meta-analysis found a mean rate of nonadherence of 31.8%, with adolescents proving to be at greater risk for nonadherence than children (Dobbels, Ruppar, DeGeest, Decorte, Van Damme-Lombaerts, & Fine, in press). However, the authors indicated that no individual study found this rate, concluding that the wide variability is likely due to the ways in which adherence is defined and measured.
While the precise rate of nonadherence is difficult to estimate, it is evident that nonadherence is a problem for many children and adolescents who have received renal transplants.

The majority of adherence research in the pediatric renal transplant population focuses on adherence to immunosuppressant medication due to its vital importance. Research suggests that nonadherence to immunosuppressant medication is a primary cause of negative health outcomes in renal transplant recipients. Specific outcomes that are typically measured include graft loss, rejection, and death (Fredericks et al., 2008; Nevins, Kruse, Skeans, & Thomas, 2001; Sudan, Shaw, & Langnas, 1998). Both types of rejection, chronic and acute, can result in graft loss, which is the loss of the new kidney tissue (Matas et al., 2002). Once total graft loss has occurred the patient will need to return to dialysis and, ultimately, get another kidney transplant.

One larger study looking at adult renal transplant patients found a strong relationship between adherence and health outcomes. The authors enrolled 267 patients immediately following transplant. The patients were then given electronic monitors to track their usage of immunosuppressant medications for the first 6 months following transplant. Outcome measures used included: acute rejection episodes, graft loss, and death. In this study, the oral medication that was prescribed had relatively simple dosing, meaning that the patients took only one or two pills per day. The authors found that, on average, patients took their medication 95% of the time. They propose that this high percentage is likely due to the ease of the medication regimen for these particular patients. However, despite high rates of adherence, the authors found a direct association between adherence and health outcomes. Patients who had a declining rate of adherence
over the 6 months following transplant were 13.9 times more likely to have acute rejection than those who remained adherent, and 4.3 times more likely to have graft loss (Nevins et al., 2001).

Shaw, Palmer, Blasey, and Sarwal (2003) looked at rates of nonadherence in the pediatric renal transplant population, as well as the effect of nonadherence on acute rejection, chronic rejection, and graft loss. The authors used a retrospective chart review of 112 children and adolescents from a single site. In this study, adherence was determined based on documented serum levels. These were obtained from drug assays that were collected during clinic visits. In addition, indications of acute rejection, chronic rejection, and graft loss were abstracted from the patients' medical charts. Adherence was measured using drug assay levels of immunosuppressant medications. Children were considered to be nonadherent if they had consistently low levels of medication in their blood at the time of the blood draws. The authors found that adolescents had an average rate of nonadherence of 45% and children an average rate of 19%. Adherence was a significant predictor for both acute and chronic rejection of the kidney, but not complete graft loss.

One final study looking at children with renal transplants found a similar relationship between adherence and health outcomes. The authors used prescription refills as their measure of adherence and graft survival as their outcome measure. By using data from the United States Renal Data System, the authors were able to obtain a sample size of 4,086 children. Adherence was significantly related to graft survival in both children and adolescents. Over the three-year period that was studied, youth who had graft loss were twice as likely to be nonadherent to their medication regimens.
Contradictory to other research, these authors found higher rates of adherence in adolescents than in children; however, adherence rates in both groups had a significant relationship to health outcomes (Chisholm-Burns, Spivey, Rehfeld, Zawaideh, Roe, & Gruessner, 2009).

Research clearly indicates the significance of immunosuppressant medication adherence after a kidney transplant. Despite this awareness, studies continue to find that adherence is a large problem for children and adolescents who have undergone kidney transplantation. Further research would be beneficial to increase clinicians’ understanding of the reasons why people are nonadherent. This will hopefully lead to an ability to increase rates of adherence, and therefore improve health outcomes.

**Barriers That Affect Adherence in Other Populations**

Identifying barriers to adherence is the first step clinicians can take in helping patients to overcome the barriers. Some research has examined the relationship between the number of barriers and adherence rates. Research on the topic of barriers to adherence has had mixed results. However, inconsistent findings could be attributed to the definition of barriers and the manner in which they are measured.

Some of the limitations in studying barriers to adherence need to be addressed before the presented research can be fully appreciated. The definition of barriers to adherence is not consistent in the literature. The majority of studies that have explored barriers to adherence have done so in a subjective way, using qualitative methodology. In quantitative research, authors frequently choose and combine measures that are meant for purposes other than looking at barriers to adherence. While the author may be using quantitative measures, the choice of measures, and, therefore, the way barriers are
defined, is done subjectively by the authors. Measures are beginning to be developed that are looking at the topic of barriers to adherence, however, they are still early in development. It is important to have measures that look at disease-specific barriers, and do so in a reliable and valid way (Simons & Blount, 2007). Another limitation to researching barriers to adherence is the usage of both parent and child report of perceived barriers. It is best to consider data from both parent and child perspectives (Varni, Jacobs, & Seid, 2000); however, it is difficult to know if similarities and differences are rooted in true differences in perceptions or in differences in reporting. This is not a unique limitation to adherence research; however, it is one that needs to be considered when examining the literature.

Another reason research results are not consistent may be due to the fact that some researchers look strictly at the number of barriers endorsed. This method does not necessarily capture the intensity of the impact of a single barrier on a person. For example, one patient may have three barriers which only place a small burden on him, while another patient may have one barrier which is strongly prohibitive to her taking her medication. The factors involved with studying barriers to adherence point to the significance of continued research in the field of barriers to adherence.

Modi and Quittner (2006) conducted a study looking at barriers to adherence in children with cystic fibrosis and asthma. The authors compared 72 children ages 6 to 13 with cystic fibrosis or asthma. Results showed that there was no direct correlation between adherence and number of barriers endorsed by self-report. In this study, adherence was measured using three different methods of measurement: prescription refill data, daily phone diary, and electronic monitoring. Data from these three measures
was used to calculate a percentage of taken medication out of total prescribed medication for each child. Barriers were assessed using a semi-structured interview along with specific questions of 25 common barriers as perceived by the authors. Both the child and the parent were interviewed separately. The findings of this study indicated that specific barriers were determined based on disease-specific regimens; however, certain barriers were endorsed in both regimens. One common element between the two disease regimens was the need to take oral medications. The primary barrier identified for taking oral medications was forgetting. Other identified barriers for taking oral medications included: oppositional behaviors, time management, and adverse side effects. While the authors did not find a correlation between number of barriers and adherence, this study contributed valuable information on specific types of barriers that affect both parents and children. In addition, even though statistical significance was not found, the researchers did identify trends leading towards a potential relationship between barriers and adherence. According to the authors, additional research is needed to better explore these questions.

Another study looking at the relationship between adherence and number of barriers in children used a similar methodology to the previous study. The primary difference was that only caregivers were interviewed in this study. The population being studied was caregivers of children with a mean age of 5.1 years who were HIV-positive. Investigators used three methods of measuring adherence and transformed adherence into a categorical variable. They obtained data from pill counts, caregiver-reported adherence, and electronic monitoring. Percentage of adherence was then calculated based on amount of taken medication out of total prescribed medication. Groups were defined based on a
cut-off rate of 80%. Therefore, children who took 80% or more of their prescribed medications were considered adherent, and children who took less than 80% of their prescribed medications were considered nonadherent. Barriers were determined based on results from a semi-structured interview with one caregiver, in which 10 common barriers were suggested to prompt caregivers to list all barriers that affect their child. Caregivers were then given a Likert-type scale and asked to rank the extent to which they perceived the barrier to affect their children. The authors did not find a significant relationship between number of barriers endorsed and the adherence group in which the child belonged (Steele et al., 2001). An explanation for why they did not find a significant relationship could be due to a number of factors. Factors could include, but are not limited to, the way barriers were measured or specific characteristics of the illness. Another unique factor to this study is that the researchers were looking at very young children. There are likely differences between young children and older children or adolescents in perceived barriers to adherence.

While the two previously presented studies did not find a significant relationship between adherence and number of perceived barriers, many others have found a relationship between the two variables (Marhefk, 2008; Marhefk, Farley, Rodrigue, Sandrik, Sleasman, & Tepper, 2004; Simons, McCormick, Mee, & Blount, 2009; Zelikovsky, Schast, Palmer, & Meyer, 2008). An example is a study done by Logan, Zelikovsky Labay, and Spergel (2003) with 152 adolescents diagnosed with asthma in which their aim was to validate a measure for perceived barriers in adolescents. This study measured adherence using child self-report of adherence. Children completed three Likert-type questions relating to adherence. Based on the child’s response, he or she
was put into one of four categories: consistently adherent, somewhat adherent, somewhat nonadherent, and consistently nonadherent. Barriers were assessed using three different measures specific to other domains. They measured social desirability, perception of medication, and risk taking behaviors. Each of these measures was then used in association with the child’s adherence category to develop the authors’ measure. With the measure that was developed in this study, the researchers found that adherence scores correlated with the number of perceived barriers as identified by the adolescent. The most common types of perceived barriers reported in this study were represented by five domains: disease/regimen issues, cognitive difficulties, lack of social support/lack of self-efficacy, denial/distrust, and peer/family issues. While this study was done with patients with asthma, a study that was specific to solid organ transplantation identified similar domains as being the primary barriers that are reported by children and parents (Simons & Blount, 2007). The domains that were identified in both studies are larger concepts that represent more specific barriers. While some researchers find that barrier domains are similar between chronic illness populations, the specific barriers will likely vary based on disease-specific aspects of the treatment regimens. Therefore, looking at different chronic illness populations may be beneficial in getting a broad understanding of barriers to adherence; however, in order to examine specific barriers it is necessary to consider each illness and treatment regimen separately.

**Barriers That Affect Adherence in Renal Transplant Recipients**

A recent study examining pediatric renal transplant recipients examined the relationship between adherence and perceived barriers to adherence. In this study, a significant relationship between adherence and perceived barriers to adherence was not
found. Adherence was measured by using adolescents’ self-reported data and immunosuppressant drug assay data. Perceived barriers, which they classified as ‘adversities,’ were obtained through a 10-item measure created by the author that was given to 33 adolescents. Insignificant results were obtained when comparing adherence to an overall adversity score. However, when looking at specific barriers, certain ones correlated better with adherence than others. According to self-reported adherence, the barriers of taking medication and talking with others were associated with adherence if significance is defined as p<.10. When using drug assay levels as the measure of adherence, the barriers of medical procedures, missing school, and feeling scared about what might happen were also significantly related to adherence if significance is defined as p<.10 (Ratcliff, Blount, & Mee, 2010). The differences found in terms of which adversities are significantly related to adherence shows the impact that the measure of adherence has on final outcomes. Both of these measures of adherence have definite weaknesses. In addition, the measure used to determine adversities is based purely on clinical experience of the researcher and does not have established reliability or validity. While this study has clear weaknesses, it is one of few that examines the relationship between barriers to adherence and adherence in the pediatric renal transplant population.

Another study that examined perceived barriers to adherence in youth who had undergone kidney transplantation was done by Zelikovsky et al. (2008). The researchers measured both adherence and perceived barriers in 55 adolescents ranging from 11 to 18 years of age. Adherence was measured using the Medication Adherence Measure (MAM), which is a self-reported measure of adherence. Relatively high rates of adherence were found, which may be due to the fact that self-reported adherence is
typically over reported (Quittner et al., 2007). Of the adolescents studied, 21.8% were considered to be nonadherent. In this study, nonadherence was defined as missing more than 20% of scheduled doses. Barriers were assessed using a variety of self-reported measures. The authors measured potential barriers such as knowledge of the regimen, time of day the medication was to be taken, and medication management. Correlations were found between nonadherence and several different types of barriers that the authors investigated. The most common perceived barrier for taking oral medication was forgetting. Not surprisingly, when medication management was done primarily by the adolescent’s parent(s), reported rates of adherence were the highest (Zelikovsky et al., 2008). The findings presented in this study regarding common types of barriers may be helpful for clinicians to effectively intervene with patients. For example, forgetting was the most commonly reported barrier; therefore, forgetting is an area to explore with patients who are having difficulties with adherence. In this example, the clinician can then aid with developing strategies to combat the problem, such as putting up written reminders or setting an alarm.

A recent study by Simons and colleagues (2009) also looked at barriers to adherence for adolescents with renal transplants. These authors also used the MAM to measure adherence, but added drug assay data from the past year. Assays are routinely done during clinic visits and are recorded in the patient’s medical chart. For the purpose of this study, a chart review was done in order to abstract the assay values. The less stable the amount of medication in the blood, the lower adherence is assumed to be. The investigators used the data obtained from the drug assay chart review along with the MAM and developed a system of categorizing adherence into four groups: those who
report high adherence and have acceptable drug levels, those who report high adherence and have drug levels outside of the acceptable range, those who report non-adherence and have acceptable drug levels, and those who reported non-adherence and have unacceptable drug levels. Barriers were determined by an interview conducted over the phone, which consisted of open-ended questions. Multiple coders then coded the responses. After qualitative analysis, four primary themes of barriers to adherence emerged: forgot/distracted, poor planning/scheduling issues, physical barriers/medication issues, and voluntary resistance/attempts to be normal. Adolescents and their parents both indicated that poor planning and scheduling problems were their largest barriers. In addition, the authors found that the overall number of barriers reported by both parents and adolescents were significantly higher in the nonadherent group than in the adherent group, concluding that number of perceived barriers is related to level of adherence.

Many studies that investigate barriers to adherence collect data from both the parent and the child or adolescent. Studies have varied in the amount of discrepancy found between child and parent report. While some research has found that children and parents perceive barriers similarly, others have found that children and parents appear to see barriers differently. Frequently authors do not report which group is identifying the specific barrier as significant or only make small mention of it (e.g. indicating that it is the parent who is saying that it is a barrier for the child). Due to the fact that each person has individual insight and contributes to the adherence process, it may be beneficial to more closely examine both persons' perception of barriers.

Significance of Parent-Child Interconnectedness

Adherence is more than a single obstacle to overcome and involves more than one
person. The process of being adherent involves many different dimensions, especially in children and adolescents. One important component to adherence for children and adolescents is the parent-child relationship (De Civita & Dobkin, 2004). The way the parent and child interact in regards to adherence to the treatment regimen is essential to make positive health outcomes for the child.

A study done with adolescents who had undergone liver transplantation looked at parent and child psychological functioning, as well as overall family functioning. The authors then looked at the relationship of both the parent and child’s psychological functioning and family functioning with the degree of the child’s adherence (Fredericks, Lopez, Magee, Shieck, & Opipari-Arrigan, 2007). As has been consistent with other research (Williams, Laffel, & Hood, 2009), Fredricks et al. (2007) found that adherence rates correlated with better parent and child psychological functioning, as well as better family functioning.

The relationship between the parent and child is an important factor to consider when researching adherence behaviors. The parent-child relationship has been shown to predict many risk-taking behaviors, including health-related behaviors. For example, a study done with children who were HIV-positive found that when the child perceives his or her relationship with a parent as a good relationship, the number of undesirable behaviors decreases (McBride et al., 2005). The perceived level of connectedness between the parent and child may be particularly important when a child has a chronic illness due to the fact that research has shown that both parents and children perceive a child’s illness as a shared entity among the family (Beveridge, Berg, Wiebe, & Palmer, 2005).
Despite the fact that both parents and children considered the child’s illness to be a shared entity, they did not have high agreement on what were the most stressful components of the illness. In the study done by Beveridge and colleagues (2005), parents and children agreed on 20% of the items when asked to identify the most stressful part of having a chronic illness for the child. The low rate of agreement indicates that even though parents and children are sharing ownership of the illness, they are not viewing the difficulties involved in the same way. The disagreement could be problematic when clinicians are attempting to work with both the parent and child to increase adherence. Clinicians should keep in mind that each report may give different information, but they should not minimize either person’s perception of the difficulties involved with adhering to the treatment regimen. Both perceptions are valuable since the parent and child are sharing in the experience of the chronic illness and in the adherence process. In addition, reports of children’s behaviors by parents and children have been found to indicate different concerns. Both are considered to be valid, and, therefore, each should be considered when looking at children’s behaviors (Kamphaus & Frick, 2005).

Much of the research that is conducted on perceived barriers to adherence is done looking at barriers for the child. When parents are involved in the research, they are reporting on their perception of what the child perceives as a barrier to adherence. Research that looks at both parent and child report needs to consider the specific type of information that is being sought. Children self-report a higher number of internalizing problems, while parents report higher levels of externalizing problems in their children (Kamphaus & Frick, 2005). When the information being obtained is more objective, rather than subjective, parents and children have higher rates of agreement. For example,
reporting on the number of doses the child misses is a more objective report than asking the parent why the child is not adhering. This is because the second piece of information that is being asked is a thought, feeling, or attitude within the child, where as the first is simply a behavior. When comparing parent and child reports of problems involving the child, it is found that the lowest rate of agreement is on issues that surround what is going on inside of the child. Therefore, areas such as motor functioning, or other concrete, objective measures should not have much discrepancy between parent and child report. However, when it comes to the child’s perception of his or her world, parents and children have low rates of agreement (Verhey et al., 2009).

Beyond barriers to adherence, there are many other areas of research that involve variables that are within the child. Quality of life has been more highly researched than perceived barriers to adherence and also falls into the domain of the child’s perception of his or her world. A study by Eiser and Morse (2001) examined all available measures of health-related quality of life. After a review of the literature, the authors pointed to the significance of both child and parent-report of the child’s experience. The authors concluded that each report is necessary to fully understand quality of life in the child; however, there is a discrepancy between parent and child reports. The authors identified multiple factors as potentially leading to this discrepancy, including: parents’ perception of normal development, parents’ expectation and hopes for their children, other life stressors, and parents’ mental health. The authors point to the need of exploring the reasons for the variability between the parent and child’s perceptions further. They state that each report has independent value and each needs to be better understood. However, their primary call for additional research is to understand what the discrepancy between a
parent and child means in terms of outcomes for the child.

The parent-child relationship is too dynamic to study as a single entity. Therefore, in research it is necessary to look at smaller components contributing to the relationship. One component of the relationship that is salient to adherence is that of teamwork. It has been found that teamwork between the parent and child is an important factor in the outcome of adherence (Anderson, Brackett, Ho, & Laffel, 2000). Better teamwork has been shown to be related to higher levels of adherence. When a parent and child are working together in the adherence process, it would be expected that both the parent and child would perceive the child's barriers to adherence in a more similar way than those who are not working as a team. Therefore, it would be expected that children would have a greater rate of adherence if the parent and child perceive similar barriers.

A study that expands on the idea of teamwork found that collaboration is an important component to adherence. Adolescents and parents independently rated their perceptions of the degree of collaboration between them. There were three main components of collaboration, as identified by the authors: collaboration to compensate for cognitive functioning, interpersonal enjoyment, and frequency of collaboration. Enjoying collaboration was found to be the factor that contributed the most to outcome measures. As rated by both the parent and child, enjoying the process of collaboration was the best predictor of adherence to treatment (Berg, Schindler, & Maharajh, 2008). Therefore, these authors concluded that the main benefit of collaboration is an interpersonal connection between the parent and child.

An additional factor that is involved in the overall relationship between the parent and child is communication. It has been found that children value their parents' input
when dealing with serious issues. However, many children do not feel comfortable talking with their parents about important topics. When children report not feeling comfortable talking with their parents, it is found that the children display a greater number of compromised behavioral and emotional health problems (Ackard, Neumark-Sztainer, Story, & Perry, 2006). One behavioral health problem is adherence. Miller and Drotar (2007) found that parent-child communication is a predictor of adherence. In other words, findings suggest that the more the parent and child are communicating with one another, the higher the child’s adherence. When the parent and child are communicating openly, it is more likely that each will be aware of the other’s perceptions.

Examining teamwork and communication can aid researchers in understanding the importance of the relationship between the parent and child in improving the child’s adherence. Another way to examine the parent-child relationship may be to investigate the amount of discrepancy between parent and child reports, specifically their reports of barriers to adherence. It is proposed that the higher the degree of teamwork, collaboration, and, communication, the more the parent and child will perceive barriers in the same way. This notion of studying parent and child discrepancies has been somewhat used in adherence research, as well as in other domains.

A fair amount of research has been done using the Child Behavioral Checklist to examine discrepancies between parent and child report. Authors examine the extent to which discrepancies in parent and child reports affect adverse behavioral outcomes. While the outcomes that are being studied in this research are not health-related, they are adverse behaviors, just as nonadherence is an adverse behavior. The authors found that an increased discrepancy between parent and child report does, in fact, lead to long-term
predictions of risky behaviors. In addition, the authors point to the fact that the inclusion of both reports allows for a richer understanding of the child than would be obtained by only having one or the other (Ferdinand, van der Ende, & Verhulst, 2006). In most adherence research, both parent and child report are obtained even when they are not reported on independently. Research in the CBCL literature may help researchers to shed greater light on information that is already being obtained in adherence research.

In addition to research using the CBCL, there has been some research looking at the significance of discrepancies in the area of adherence. Research has been conducted looking at the discrepancy between parent and child report of allocation of treatment responsibilities. Several studies have found that adolescents report higher levels of autonomy and competence in diabetes management than their parents report (Mansfield, Addis, Laffel, & Anderson, 2004). Other research takes it a step further and relates the significance of the discrepancy between parent and child report to the child’s health outcomes. A study by Anderson and colleagues (1990) found that there was poorer metabolic control when there was a greater discrepancy between mother and child report of who is responsible for tasks of diabetes management.

One study of 189 adolescents who have been diagnosed with Type 1 diabetes mellitus examined many different factors that may be associated with parent-child discrepancies. In this study, adherence was measured using self-report data from the adolescent, mother, and father. The level of parent involvement in a variety of diabetes-related tasks was then assessed using a self-reported measure of diabetes responsibility and conflict. In addition, the child and parents’ perception of the adolescent’s competence and resourcefulness was measured using a self-report measure. There were several other
factors also measured in this study. An overarching theme was that there were significant discrepancies between the adolescent, the mother, and the father. In fact, the authors determined that the greater the discrepancies between the adolescent and parent, the poorer the adolescents’ diabetes management and health outcomes. This was significant for factors related to health outcome, but also for child and parent, particularly mother, well-being. These authors point to the fact that this is likely due to the autonomy that adolescents are seeking, which can be beneficial in the long-term, but has poor health consequences in the short term (Butner, Berg, Osborn, Butler, Godri, Fortenberry et al., 2009). One goal of research needs to be to identify where interventions can be effective in order to promote autonomy but also not jeopardize the child’s health.

Research looking at the parent-child relationship based on congruence of self and parent report has been limited thus far. In the barriers to adherence literature, the significance of the parent-child relationship has not yet been explored. Overall, the mutual understanding of the child’s barriers to adherence has been neglected. Research has pointed to the importance of the parent-child dyad, specifically in communication and collaboration between the parent and child. Based on current family systems literature, it seems likely that the relationship between the parent and child affects behavioral outcomes of the child. Understanding if congruence between the parent and child report of perceived barriers to adherence plays a role in behavioral outcomes, particularly adherence, will expand the current literature.
Chapter II: Rationale and Hypotheses

In the past fifty years, advancements in immunosuppressant medication have allowed transplantation to become a viable treatment option for children with end-stage-renal-disease (ESRD) (Hatch & Agrawal, 2009). Transplantation has substantially increased the long-term survival of children with ESRD but the oral medication regimen that follows transplant requires ongoing management. Adherence to the immunosuppressant medication regimen is difficult. However, high levels of adherence are essential for optimal health outcomes since advances in medicine are only as beneficial as the extent to which the patient follows through with his or her treatment regimen.

Research with children who have undergone renal transplantation indicates that nonadherence can result in negative health outcomes, with decreased adherence being associated with increased rates of kidney rejection and death (Shaw, Palmer, Blasey, & Sarwal, 2003). Despite serious health outcomes, average rates of nonadherence in pediatric renal transplant recipients have been found to be approximately 32%, with some studies finding rates of nonadherence as high as 75% (Dobbels, Damme-Lombaert, Vanhaecke, & De Geest, 2005; Dobbels, Ruppar, DeGeest, Decorte, Damme-Lombaerts, & Fine, 2010). Despite that fact that there are high rates of nonadherence and severe negative health outcomes that can result from nonadherence, specific barriers to adherence are not well established. Similarly, research is conflicted on the importance of
reducing the number of barriers (Modi & Quittner, 2006; Simons, McCormick, Mee, & Blount, 2009; Steele, Anderson, Rindel, Dreyer, Perrin, Christensen et al., 2001; Zelikovsky, Schast, Palmer, & Meyer, 2008). A better understanding of the relationship between the number of barriers for the child and adherence would help to identity patients at risk for poorer adherence.

For children and adolescents, achieving adherence is not a task that is only relevant for the child. When a child has a chronic illness, the entire family is typically involved in the management of the regimen (Beveridge, Berg, Wiebe, & Palmer, 2005). Reports from both the parent and child’s perceptions of the barriers that the child faces to adherence allow for a more thorough assessment and formation of effective interventions to address barriers to adherence. Therefore, the following hypotheses are as follows: (1) Increased number of barriers (as measured by the Parent Medication Barriers Scale [PMBS]) will predict poorer rates of adherence (as calculated from the MEMS bottle), (2) Increased number of barriers (as measured by the Adolescent Medication Barriers Scale [AMBS]) will predict poorer rates of adherence (as calculated from the MEMS bottle).

Beyond looking at parent and child report separately, additional information may be obtained by exploring the relationship between the two reports. The degree to which there is congruence in the way that parents and children see adherence barriers may be indicative of many different components of the parent-child relationship, such as communication, teamwork, and collaboration. All of these components have been found to be significantly related to adherence (Anderson, Brackett, Ho, & Laffel, 2000; Berg, Schindler, & Maharajh, 2008; Miller & Drotar, 2007). If the discrepancy between parent and child reports is indicative of many of the parent-child relationship factors that have
been found to be predictive of adherence, then looking at the discrepancy between parent and child-report would give clinicians the opportunity to screen for potential adherence problems, as well as better understand on what level to intervene. Additional support for looking at the discrepancy between parent and child report is that research in other fields of psychology has found that discrepancies between parents and children in reporting behavioral problems are associated with adverse behavioral outcomes for the child (Ferdinand, van der Ende, & Verhulst, 2006). The significance of the discrepancy between parent and child perceptions of the child’s barriers to adherence has not yet been researched. Therefore, the third hypothesis is as follows: Larger discrepancies between parent and child report of barriers to adherence (as measured by the PMBS and AMBS, respectively) will predict poorer rates of adherence (as calculated from the MEMS bottle).

In order to achieve a comprehensive understanding of the barriers that children face, the final part of this study will be a secondary analysis that will descriptively investigate the most prevalent barriers to adherence for the child as perceived by the parent and the child. While the detailed analysis of specific barriers to adherence will be descriptive in this study, it will help direct future research in the area of barriers to adherence both in terms of which barriers are frequently endorsed by parents and children and which barriers have the greatest degree of congruence between parents and children.
Chapter III: Method

Participants

This study, using data abstracted from an anonymous database, will involve 40 children who have undergone kidney transplantation at Cincinnati Children’s Hospital Medical Center (CCHMC), as well as one caregiver per child. The patients are between the ages of 7 and 17-years-old, inclusively. Patients were previously recruited from the Division of Nephrology at CCHMC for a larger study done through the Center for the Promotion of Adherence and Self-Management. The larger study was conducted under the approval of the Institutional Review Board at CCHMC.

The sample size in this study is consistent with much of the adherence literature, particularly studying this specific population. With the analyses that will be used, in order to maintain a power of 0.80 while using an alpha level of .05, an effect size of .37 will be necessary to find significant results due to the predetermined sample size. Based on the statistic being calculated, an effect size of .37 is representative of a medium effect needed to find significant results. It is anticipated that it is feasible to obtain significant results with a medium effect size, as other studies using this population with similar sample sizes have found significant results. It is recognized that the degree of familywise error will be somewhat high if all statistical analyses use an alpha level of .05 to determine significance. However, due to limitations of sample size, using this alpha level is sufficient given that this study is relatively novel and ones of its primary purposes is to
describe the importance of the relationship of parent and child report of barriers to adherence and to provide guidance for future research.

**Measures**

**Demographic factors.**

Demographic factors were obtained for each child using a form that was completed by the parent. This included factors such as child’s age, sex, race/ethnicity, time since transplant, age at transplant, and total family income. Demographic statistics will be reported in the final document. The primary information obtained from this form that will be used for analyses will be age of the child at the time of participation in the study.

**Medication Event Monitoring System (MEMS).**

In order to measure adherence, the Medication Event Monitoring System (MEMS) was used. The MEMS bottle has a pressure-activated microsensor that records the time and frequency at which the bottle was opened. It was given to each of the participants in order to digitally track medication usage for one month, as measured by opening the bottle. It was assumed that when the bottle was opened, the correct dosage of medication was taken. Due to cost and feasibility restrictions, each child, in collaboration with the researcher, identified one medication to be transferred to the MEMS bottle. The child was instructed to place the identified medication in the bottle and take it only from the MEMS bottle for the one month following the date that the self-report measures were completed. The cap of the bottle had a device inside of it, which stored the data. After the bottle was returned to the investigator, the data was downloaded. An adherence score was then calculated. The first step in calculating the adherence score was determining the
number of doses taken in the one-month period, not to exceed the total prescribed dose on an individual calendar day. This number was then divided by the total number of prescribed doses over the month period and multiplied by 100 to get a total adherence percentage. One study examining the usage of the MEMS bottle with pediatric transplant populations, found many problems with this form of measurement of adherence. Problems included, but were not limited to: refusal to participate due to not wanting to use the bottle, inconvenience for the family, and a change in routine while using the MEMS bottle (Shellmer & Zelikovsky, 2007). However, in the larger study in which data for the proposed study will be obtained, these same barriers to using the MEMS bottle were not identified by participants. As a whole, the MEMS bottle has drawbacks, including malfunctioning and losing data, however, when working properly electronic monitoring is currently considered to be the most accurate measure of adherence available according to conclusions from a conference featuring many of the leading researchers in the field, as well as from an extensive review of the current literature (Fine et al., 2009; Quittner et al., 2007).

**Parent Medication Barriers Scale (PMBS).**

The Parent Medication Barriers Scales (PMBS) is a proxy-report of parent’s perception of the child’s barriers to adherence that is completed by a parent or primary caregiver. It consists of a 5-point Likert-like scale ranging from ‘strongly disagree’ to ‘strongly agree’ and is used to assess a variety of different barriers to medication adherence. This measure was developed specifically to quantitatively measure barriers for children who have undergone solid organ transplantation as perceived by a caregiver.
The initial formation of the measure was done using a factor analysis with Varimax rotation of 19 potential barriers that the authors identified as relevant to this population (Simons & Blount, 2007). The list of 19 barriers was a reduction from the initial 39 barriers. The 20 items that were eliminated were based on 90% or more of participants not endorsing the barrier as relevant, as well as one item dropped due to item-total correlations. After the factor analysis was completed, four additional barriers were removed from the measure due to significant loading on other barriers. Within the remaining 16 barriers, there were four factor domains identified: “Disease Frustration/Adolescent Issues”, “Regimen Adaptation/Cognitive Issues”, “Ingestion Issues”, and “Parent Reminder”.

In order to examine construct validity, Simon and Blount (2007) did several correlations between subscales of the measure and demographic, disease, and family factors. There were no significant differences found based on age, developmental delay, gender, race, income, or parents’ educational background. There were also no differences found based on health care coverage, prescription drug coverage, or type of transplant. The less time that had elapsed since transplantation and the greater the number of medications the child was taking significantly correlated with higher scores on the subscale, “Ingestion Issues”. In addition, more frequent and intense side effects were correlated with higher scores on the subscale, “Disease Frustration/Adolescent Issues”, and total PMBS score. Using an analysis of variance, the authors found that the “Parent Reminder” subscale was significantly lower when the child and parent both agreed that the parent was primarily responsible for the child’s medication regimen. Additionally, higher scores on the “Parent Reminder” subscale were also associated with lower levels
of child knowledge. When parent knowledge was lower, there were significantly higher scores on the subscales, “Disease Frustration/Adolescent Issues” and “Ingestion Issues”. While this measure has not yet been published in research beyond that of the original study, preliminary construct validity is promising.

In order to establish criterion validity, adherence was used as the criterion to compare the measure. Simons and Blount (2007) used a self-report measure of adherence and an immunosuppressant drug assay to measure adherence. The authors categorized the patients into four groups based on results from both the self-report of adherence and the drug assay: “Genuinely Adherent”, “Deniers/Medically Complicated”, “At Risk”, and “Genuinely Nonadherent”. Both “Genuinely Adherent” and “Deniers/Medically Complicated” were considered to be adherent based on the self-report measure of adherence. A child was determined to be adherent according to the self-report measure of adherence when both the parent and the child reported less than 10% of doses being missed in the past week. The “Genuinely Adherent” and “At Risk” groups were found to be adherent according to the drug assay level, meaning that the child’s medication levels were within the therapeutic range. The authors did not find a significant difference between the two adherent groups according to self-reported adherence: “Genuinely Adherent” and “Deniers/Medically Complicated”. There was also no significant difference between the two nonadherent groups according to self-report: “At Risk” and “Genuinely Nonadherent”. There were several differences detected between the adherent groups and nonadherent groups across all subscales, besides “Parent Reminder”. The group that reported the fewest barriers was the “Deniers/Medically Complicated” group and the group that reported the most barriers was the “At Risk” group. Among reports of
the “Deniers/Medically Complicated” group and the two self-reported nonadherent
groups significant differences were found in the total score, the “Disease
Frustration/Adolescent Issues” subscale, and the “Regimen Adaptation/Cognitive Issues”
 subscale at the alpha level of p<.05. Total barriers and the subscales, “Regimen
Adaptation/Cognitive Issues” and “Ingestion Issues” were found to be significantly lower
in the “Genuinely Adherent” group than in the “Genuinely Nonadherent” group at the
alpha level of p<.10. There were also significantly fewer items reported on the subscale,
“Ingestion Issues”, in the “Genuinely Adherent” group versus the “At Risk” group at the
alpha level of p<.10. Using adherence as the criterion to validate this measure, it was
found that there were significant differences in the expected direction for the measure’s
total score and subscale scores when comparing groups determined by adherence.

Adolescent Medication Barriers Scale (AMBS).

The Adolescent Medication Barriers Scale (AMBS) is a self-report measure used
for adolescents to identify barriers to adhering to their medication regimen. It is a 5-point
Likert-like scale ranging from “strongly disagree” to “strongly agree.” This measure was
developed in conjunction with the PMBS in order to obtain a quantitative measure of
barriers to adherence that adolescents face from their own perspective.

The AMBS was developed in much the same way as the PMBS with only slight
variations. For this measure, the authors began with 29 original items and reduced the
number to a total of 17 items (Simons & Blount, 2007). The reasons for the decrease in
items included: not being endorsed by enough children, item-total correlations, and
loading on other barriers. After factor analysis with Varimax rotation, the final scale
consisted of 17 total items. The AMBS consisted of only three subscales: “Disease
Frustration/Adolescent Issues", “Regimen Adaptation/Cognitive Issues”, and “Ingestion Issues”. Twelve of the items were the same as those in the PMBS with only slightly different wording. However, they did not all load on the same factors equally. This is important to recognize due to the fact that while the subscales on the PMBS and AMBS have the same names, they do not represent the same items, and are, therefore, not identical in the construct that is being captured.

Validity was determined for the AMBS in the same ways that were done for the PMBS. It had similar correlations between factors and subscales, indicating that the subscales are measuring what they are intending to measure. In addition, the authors measured the criterion validity by using the same four adherence groups as the PMBS. For the AMBS, there were also significant differences found between at least one of the self-reported adherent and nonadherent groups for all three subscales, as well as the total score. The validity of this measure is promising for use in children who have undergone solid organ transplantation.

The AMBS was developed for adolescents who have undergone solid organ transplantation. The primary reason both the AMBS and PMBS were developed was to quantitatively measure barriers to adherence in this population. Simons and Blount (2007) developed both of these measures with the child’s age range being from 11 to 21 years of age. The larger study in which data for the proposed study was obtained expanded the age range to the inclusion of 7-year-olds and older. Seven-year-olds have been found to be reliable sources of self-report (Riley, 2004) and neither the PMBS nor AMBS address barriers that would only pertain to children older than 11 years of age.
Procedure

The proposed study will be executed after obtaining Institutional Review Board approval through Xavier University, using data that was collected from the larger study that was conducted at CCHMC. The original self-report information was obtained as part of a series of measures that were given to both the child and the caregiver. Participation, including consent and time for the child and parent to fill out self-report measures, took approximately one hour and was typically done directly after a clinic visit in order to minimize inconvenience for patients and their families. The MEMS bottle was given to the patient at the time the self-report data was completed. Patients were asked to put one of their immunosuppressant medications into the MEMS bottle and use only that bottle for the following 30 days. They were also instructed to only take a single prescribed dose out of the bottle each time it was opened. The bottle was then collected, either at a future clinic visit or mailed back to CCHMC by the family, and data was downloaded.
Chapter IV: Proposed Analyses

The proposed study will consist of three primary hypotheses being statistically tested, followed by a descriptive item-by-item analysis. All three of these hypotheses will be tested by calculating regression coefficients. The descriptive analysis will examine each barrier and how parents versus children perceive the barrier. In addition, a table will be presented in the final analyses reporting correlation coefficients between all measures being used in the following proposed analyses.

Child’s age has been found to be associated with adherence (Dobbels et al., 2005). The first step for all of the analyses will be to determine if the child’s age is related to adherence. In order to account for the amount of variance explained by child’s age, or the influence that age has on adherence, child’s age will potentially be statistically controlled for in this study. A correlation coefficient will be calculated to determine if child’s age is significantly correlated with adherence in this specific population. A Pearson’s correlation coefficient will be calculated and the resulting correlation will be determined to be significant if alpha is less than .05 (p<.05). If the resulting correlation is significant, then child’s age will be controlled for in the following analyses by using a hierarchical multiple regression with age being entered into the regression equation in Block 1, followed by the independent variable being entered into Block 2. This statistical analysis will provide the amount of variance being explained by the independent variable after the amount of variance that is accounted for by age is removed. If age is not significantly
related to adherence, then a simple linear regression will be calculated for each of the following analyses.

Hypothesis 1 states: Increased number of barriers (as measured by the PMBS) will be associated with poorer rates of adherence (as calculated from the MEMS bottle). A regression coefficient will be calculated to test this hypothesis. The purpose of this analysis is to determine the extent in which the number of the child's barriers as perceived by the parent (independent variable) is associated with the child’s adherence (dependent variable). The regression coefficient will be determined to be significant if the alpha level is less than .05 (p<.05). The PMBS consists of five responses ranging from strongly disagree to strongly agree, which will be scored using a Likert-like scale. ‘Strongly Disagree’ will be assigned a 1 through ‘Strongly Agree’ which will be assigned a 5. A total score will then be calculated by summing the individual items. Higher total score indicates more barriers. The parent’s total scores will be compared to the child’s adherence score, which will be calculated using data from the MEMS bottles.

Hypothesis 2 states: Increased number of barriers (as measured by the AMBS) will be associated with poorer rates of adherence (as calculated from the MEMS bottle). A regression coefficient will be calculated to test this hypothesis. The purpose of this analysis is to determine the extent in which the number of barriers as indicated by the child (independent variable) predicts the child’s adherence (dependent variable). Scoring and analysis will be conducted in the same manner used for testing hypothesis 1.

Hypothesis 3 states: Larger discrepancies between parent and child report of barriers to adherence (as measured by the PMBS and AMBS, respectively) will be associated with poorer rates of adherence (as calculated from the MEMS bottle). This
hypothesis will be tested in a similar manner as the two prior hypotheses; however
discrepancy scores will first need to be determined. In order to determine the discrepancy
score, the 12 items that are on both the PMBS and AMBS will be used. First, both a child
and parent discrepancy index score will be calculated. The proposed study will be done
using a methodology similar to that used by Christensen, Sullaway, and Margolin in a
study looking at discrepancies between mothers and fathers’ reports of children’s
behaviors (1992). In the proposed study, the parent discrepancy index will consist of the
number of items that the parent endorsed (i.e. responded either ‘Agree’ or ‘Strongly
Agree’), but that the child did not endorse (i.e. responded either ‘Neutral,’ ‘Disagree,’ or
‘Strongly Disagree’). Conversely, the child discrepancy index will consist of the number
of items that the child endorsed as a barrier, but that the parent did not endorse. First a
between-subjects t-test will be used in order to determine if the child discrepancy index
and the parent discrepancy index are significantly different from one another. This will be
done using the child group and the parent group as two independent groups and specific
parent-child dyads will not be paired for this portion of the analysis. Then, a regression
coefficient will be calculated for both the parent and child discrepancy scores to
determine the extent to which the discrepancy scores are associated with adherence. Both
of these analyses are important, as they will show whether the child discrepancy score,
the parent discrepancy score, or both discrepancy scores are significantly related to
adherence. This allows for an examination of both the relationship between adherence
and the discrepancy of parent and child perception of the child’s barriers, as well as the
importance of whether it is the parent or the child who is endorsing more barriers when
the other is not endorsing the barriers. Significance will be determined if the alpha level for the regression coefficient is less than .05 (p<.05).

Due to limited sample size, it is not possible to do a complete statistical analysis of the item-by-item differences between parent and child report. However, this information could be beneficial to add to the literature on barriers to adherence in youth who have undergone renal transplantation. Therefore, a descriptive analysis will be conducted in order to guide future research on the topic.

Responses to each item that appears on both the PMBS and AMBS will be entered into a parent-child agreement table. Table 1 shows an example of a parent-child agreement table and a separate one will be made for each of the 12 items that appear on both the PMBS and AMBS. ‘Strongly Agree’ and ‘Agree’ will be combined to be considered endorsing the item and ‘Strongly Disagree’ and ‘Disagree’ will be combined to be considered not endorsing the item. ‘Neutral’ will be considered separately from the other two categories. A percentage will be calculated for each cell of the table. Once the table is complete, the percentages of both parent and child agreeing (A), disagreeing (B), or being neutral (C) will be summed to form a total percentage of agreement. The total percentage will show which items have higher and lower agreement between parent and child reports. This descriptive analysis will provide information regarding which barriers are more highly endorsed by parents versus children, as well as which items they endorse similarly.
References


of the cognitive and relational functions of collaboration and adjustment in dealing with type 1 diabetes. *Journal of Family Psychology, 22*, 865-874.


Shaw, R. J., Palmer, L., Blasey, C., & Sarwal, M. A. (2003). A typology of non-


Table 1

*Parent-Child Agreement Table*

<table>
<thead>
<tr>
<th>Item 1</th>
<th>Agree</th>
<th>Disagree</th>
<th>Neutral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree</td>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disagree</td>
<td></td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td></td>
<td></td>
<td>C</td>
</tr>
</tbody>
</table>

*Note.* Total agreement score = A+B+C
Appendix A

The Parent Medication Barriers Scale (PMBS) is protected by copyright so it is not reproduced in this document. The measure is available by contacting the developing author, Laura E. Simons, at laura.simons@childrens.harvard.edu.
Appendix B

The Adolescent Medication Barriers Scale (AMBS) is protected by copyright so it is not reproduced in this document. The measure is available by contacting the developing author, Laura E. Simons, at laura.simons@childrens.harvard.edu.
Chapter V: Dissertation

Abstract

Nonadherence to immunosuppressant medications following renal transplantation can lead to devastating health consequences. In order to minimize nonadherence-related negative health outcomes in children, this study aimed to identify the predictive power of the number of barriers to adherence to adherence outcomes as reported by both the parent and child. Additionally, this study aimed to determine the significance of the relationship between the parent and child’s perspectives by examining the discrepancy between reports and its ability to predict adherence outcomes. Forty-one children and their caregivers participated, with children’s ages ranging from 7 to 18 with a mean of 15. Results of the Parent Medication Barriers Scale (PMBS) and the Adolescent Medication Barriers Scale (AMBS) were used for analyses, as well as electronic monitoring data to measure adherence. The average rate of adherence from the electronic monitoring data in this sample was 79.3%. Findings indicate that number of barriers according to both parent ($p = .904$) and child ($p = .393$) reports are not predictive of adherence. Nor is the discrepancy between parent ($p = .950$) and child ($p = .902$) report predictive of adherence. Qualitative analysis of specific barriers suggests that parents and children do not consistently indicate the same barriers to adherence for the child. Although the number of barriers to adherence was not found to be predictive of oral medication
adherence, additional exploration of specific barriers to adherence as indicated by both parents and children is suggested for future research.
Barriers to Medication Adherence Following Pediatric Renal Transplantation: The Utility of Independent and Interrelated Parent and Child Reports

Each year, an average of 5,700 children and adolescents under the age of 18 are living with the diagnosis of end-stage-renal-disease (ESRD) (Government Accountability Office, GAO, 2007). Modern advancements in immunosuppressant medications are allowing children with ESRD to live well into their late adult years after having a kidney transplant (Rodriguez & Sobel, 2003). However, as medical advancements increase survival, they also present new challenges for patients, families, and clinicians. After undergoing renal transplantation there are many components involved in the treatment regimen. Three areas of primary significance are: attending clinic visits, completing lab work, and taking oral medications. In the months following transplantation, children have multiple clinic and lab visits every week, with decreasing frequency as they move further from transplant. The other significant component, taking oral medication, is particularly difficult for children who have undergone renal transplantation due to the fact that there are a large number of medications that are given at different times throughout the day and have a variety of side effects. Immunosuppressant medications are vital following transplantation and all children will continue to take at least one for the remainder of their lives. However, dosages are constantly being changed based on the level of absorption to assure the most effective dose. Dosages can be changed as often as several times per week and families are expected to understand and keep up with the ever-changing regimen (Hricik, 2003).

Despite the difficulty in maintaining the immunosuppressant medication regimen, it is of utmost importance to do so correctly. When a kidney is transplanted, the host body
recognizes the new organ as a foreign object. The host’s immune system may start to fight off the new kidney. Immunosuppressant medications weaken the host’s immune system in order to prevent it from destroying the new organ (Roche Laboratories, 1997). This is referred to as “rejection” and can happen quickly or over a prolonged period of time (Venes, 2005). Medications are constantly being altered in order to prevent rejection, while still allowing the host body to have as effective of an immune system as possible in order to prevent future illness and infection. While rejection can occur when the patient is properly taking his or her immunosuppressant medications, the risk of rejection significantly increases when the patient fails to strictly adhere to the medication regimen (Roche Laboratories, 1997).

Adherence

Traditionally, adherence is defined as “the extent to which a person’s behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice” (Haynes, 1979). Advances in medicine continue to be achieved, however, they can only be beneficial to the extent in which individuals use them properly.

There are a number of potentially negative consequences when patients do not adhere to their medication regimens. In chronically ill patients as a group, consequences of nonadherence include, but are not limited to: poorer health and the decreased well-being for the patient, up to and including death, increased cost of medical care, incorrect clinical decisions, and inaccurate conclusions in research (Rapoff, 1999).

One reason adherence is important to address in patients who have undergone renal transplantation is the cost associated with nonadherence (Pinsky, Takemoto,
Lentine, Burroughs, Schnitzler, & Slavalaggio, 2009). On average, the annual cost for a child who has a successful renal transplant is $4,916 post-transplant. However, a child with kidney failure following a transplant has an average annual cost of $41,929 (Government Accountability Office, GAO, 2007). This number includes patients who have failure due to reasons other than nonadherence; however, nonadherence is a leading cause of kidney failure following a transplant (Butler, Peveler, Roderick, Horne, & Mason, 2003). This cost affects both taxpayers and families who already have large medical expenses (Rapoff, 1999). Many of these expenses may be avoidable if the issue of adherence were more widely addressed. It needs to be addressed both in the literature, as well as in the clinical setting, as adherence should be a concern not only for patients, but also for health-care providers (Berlant & Pruitt, 2003).

Beyond the cost associated with nonadherence, there are several clinically important reasons for a child to be adherent to his or her medical regimen. While a kidney transplant may resolve ESRD, the recipient is faced with a new set of medical challenges. Research suggests that nonadherence to immunosuppressant medication is a primary cause of negative health outcomes in renal transplant recipients. Specific outcomes that are typically measured include graft loss, rejection, and death (Fredericks et al., 2008; Nevins, Kruse, Skeans, & Thomas, 2001; Sudan, Shaw, & Langnas, 1998). Both types of rejection, chronic and acute, can result in graft loss, which is the loss of the new kidney tissue (Matas et al., 2002). Once total graft loss has occurred the patient will need to return to dialysis and, ultimately, undergo another kidney transplant.

Research clearly indicates the significance of immunosuppressant medication adherence after a kidney transplant (Chisholm-Burns, Spivey, Rehfeld, Zawaideh, Roe, &
Gruessner, 2009). Despite this awareness, studies continue to find that adherence is a large problem for children and adolescents who have undergone kidney transplantation. A meta-analysis done with pediatric renal transplant recipients found rates of nonadherence to range from 5% to over 75% (Dobbels et al., 2005). A recent meta-analysis done with pediatric renal transplant recipients found a mean rate of nonadherence of 31.8%, with adolescents proving to be at greater risk for nonadherence than children (Dobbels, Ruppar, DeGeest, Decorte, Van Damme-Lombaerts, & Fine, 2010). Further research would be beneficial to increase clinicians’ understanding of the reasons why people are nonadherent. The understanding of nonadherence will aid in increasing rates of adherence, and therefore improve health outcomes.

**Barriers to adherence**

Identifying barriers to adherence is the first step clinicians can take in helping patients to overcome the barriers. Several studies have examined the relationship between the number of barriers and adherence rates. Research on the topic of barriers to adherence has had mixed results, with some studies finding that a larger number of barriers is associated with decreased adherence (Marhefka et al., 2008; Marhefka, Farley, Rodrigue, Sandrik, Sleasman, & Tepper, 2004; Simons, McCormick, Mee, & Blount, 2009; Zelikovsky, Schast, Palmer, & Meyer, 2008) and others not finding that to be a significant relationship (Modi & Quittner 2006; Steele et al., 2001).

A few studies have focused on identifying barriers to adherence specifically in the renal transplant population. As with other chronic illness populations, the findings are variable in terms of the direct relationship between the number of barriers and adherence rates (Ratcliff, Blount, & Mee, 2010; Simons et al., 2009; Zelikovsky et al., 2008), but
they also reported on the specific barriers that children and their parents endorsed. Four themes of barriers to adherence one study established were: forgot/distracted, poor planning/scheduling issues, physical barriers/medication issues, and voluntary resistance/attempts to be normal. In this study, adolescents and their parents both indicated that poor planning and scheduling problems were their largest barriers to adherence (Simons et al., 2009). While it may be important to know if the number of barriers of adherence is related to actual adherence outcomes, it may be of equal importance to understand specifically what barriers families experience.

A recent study done by Ratcliff, Blount, and Mee (2010) looked at barriers using a quantitative measure that the authors created. Although they did not find a significant relationship between total number of barriers and adherence, they did find that specific barriers were associated with adherence outcomes based on authors’ criteria of significance being defined by $p < .10$. The barriers, “having to take medication” and “difficulty talking with others about the illness” were associated with adherence (significance level = $p < .10$). When using drug assay levels as the measure of adherence, the barriers of medical procedures, missing school, and feeling scared about what might happen were also significantly related to adherence (significance level = $p < .10$). The findings from this study point to the importance of the way adherence is measured, but also indicate that a specific barrier may have a larger influence than the total number of barriers a family is experiencing.

All of the studies previously mentioned assessed both parent and child reports of adherence barriers. However, none of these studies have directly compared parent and child reports of adherence barriers. Because each person has separate insight and
contributes to the adherence process (Eiser & Morse, 2001), it would be beneficial to more closely examine both individuals’ perception of barriers.

**Parent-child interconnectedness**

In order to achieve optimal adherence for pediatric patients, many people must be involved in the process. In fact, families perceive adherence as a shared entity within the family (Beveridge, Berg, Wiebe, & Palmer, 2005), especially when the patient is a child or adolescent. One important component to adherence for children and adolescents is the parent-child relationship (De Civita & Dobkin, 2004). The way the parent and child interact in regard to adherence to the treatment regimen contributes to health outcomes for the child.

The parent-child relationship is complex, so studies operationalize it using a number of different components of the relationship, many of which have been examined within the adherence literature. A few domains that have been found to be related to adherence outcomes are: parent and child’s psychological functioning (Fredericks, Lopez, Magee, Shieck, & Opipari-Arrigan, 2007), communication (Miller & Drotar, 2007), and teamwork (Anderson, Brackett, Ho, & Laffel, 2000). The literature examining the parent-child relationship is outside the scope of this study, however, it is thought that the higher the degree of teamwork and communication, the more the parent and child will perceive barriers in the same way.

Since both parent and child reports provide unique information, it is important to use both reports when evaluating the construct (Eiser & Morse, 2001). Although it is not related to adherence barriers, some research has examined parent and child reports in relationship to one another. One study found that an increased discrepancy between
parent and child report leads to long-term predictions of risky behaviors. In addition, the
authors suggested that the inclusion of both reports allows for a richer understanding of
the child than would be obtained by only having one or the other (Ferdinand, van der
Ende, & Verhulst, 2006).

Research looking at the parent-child relationship based on congruence of self and
parent report has been limited thus far. In the barriers to adherence literature, the
significance of the parent-child relationship has not yet been explored. Overall, the
mutual understanding of the child’s barriers to adherence has been neglected. Research
has pointed to the importance of the parent-child dyad, specifically in communication and
collaboration between the parent and child. Based on current family systems literature, it
seems likely that the relationship between the parent and child affects the behaviors of the
child (Nichols, 2010). Understanding the role of congruence between the parent and child
report in behavioral outcomes, particularly adherence, will expand the current literature.

Based on the importance of adherence to oral medication for children who have
undergone renal transplantation, this study more fully explores the barriers that families
face to adhere to the child’s medication regimen. It was hypothesized that 1) increased
number of barriers will predict poorer adherence by both parent and child report and 2)
larger discrepancies between parent and child report of barriers to adherence will predict
poorer rates of adherence.

**Methods**

**Participants**

Archival data of 41 children, and one primary caregiver per child, was used for
the analyses. Inclusion criteria for the study were as follows: children were 7 to 18 years-
old, received a kidney transplant or post-transplant care, prescribed at least one orally-administered immunosuppressant medication, had at least one caregiver who speaks fluent English, child provided assent and caregiver provided consent, and an absence of cognitive deficits in both the child and participating caregiver. Four additional children and their caregivers completed measures; however, complete data sets were not available, so therefore they were not used in analyses. Demographic information for the sample is presented in Table 1.

**Procedure**

The current study was executed after obtaining Institutional Review Board approval through a university in the Midwest, using data that was collected from a larger study that was conducted at a local children’s hospital and had IRB approval through that institution. The original self-report information was obtained as part of a series of measures that were given to both the child and the caregiver. Participation, including consent and time for the child and parent to fill out self-report measures, took approximately one hour and was typically done directly after a clinic visit in order to minimize inconvenience for patients and their families. An electronic monitoring device in the form of a pill bottle, the medication event monitoring system (MEMS), was given to the patient at the time the self-report data was completed. Patients were asked to put one of their immunosuppressant medications into the MEMS bottle and use only that bottle for the following 30 days. They were also instructed to only take a single prescribed dose out of the bottle each time it was opened. The bottle was then collected, either at a future clinic visit or mailed back by the family, and data was downloaded.
Measures

**Demographic factors.**

Demographic factors were obtained for each child using a form that was completed by the parent. This included factors such as child’s age, sex, race/ethnicity, time since transplant, age at transplant, and total family income. Demographic statistics are reported in Table 1. Age of the child at the time of study participation was the only information used from this form for the current study analyses.

**Medication Event Monitoring System (MEMS).**

In order to measure adherence, the Medication Event Monitoring System (MEMS) was used. The MEMS bottle has a pressure-activated microsensor that records the time and frequency at which the bottle was opened. It was given to each of the participants in order to digitally track medication usage for one month, as measured by opening the bottle. It was assumed that when the bottle was opened, the correct dosage of medication was taken. Due to cost and feasibility restrictions, each child stored one medication, identified by the study team, in the MEMS bottle. The child was instructed to place the identified medication in the bottle and take it only from the MEMS bottle for the one month following the date that the self-report measures were completed. The cap of the bottle had a device inside of it, which stored the data. After the bottle was returned to the investigator, the data was downloaded. An adherence score was then calculated. The first step in calculating the adherence score was determining the number of doses taken in the one-month period, not to exceed the total prescribed dose on an individual calendar day. This number was then divided by the total number of prescribed doses over the month period and multiplied by 100 to get a total adherence percentage. One study
examining the usage of the MEMS bottle with pediatric transplant populations, found many problems with this form of measurement of adherence. Problems included, but were not limited to: refusal to participate due to not wanting to use the bottle, inconvenience for the family, and a change in routine while using the MEMS bottle (Schellmer & Zelikovsky, 2007). However, these same barriers to using the MEMS bottle were not identified by participants in this study. As a whole, the MEMS bottle has drawbacks, particularly malfunctioning and losing data. However, when working properly, electronic monitoring is currently considered to be the most accurate measure of adherence available according to conclusions from a conference featuring many of the leading researchers in the field, as well as from an extensive review of the current literature (Fine et al., 2009; Quittner et al., 2007).

**Parent Medication Barriers Scale (PMBS).**

The Parent Medication Barriers Scales (PMBS) is a proxy-report of perception of the child’s barriers to adherence that is completed by a parent or primary caregiver. It consists of a 5-point Likert-like scale ranging from ‘strongly disagree’ to ‘strongly agree’ and is used to assess a variety of different barriers to medication adherence. This measure was developed specifically to quantitatively measure barriers for children who have undergone solid organ transplantation as perceived by a caregiver.

The initial formation of the measure was done using a factor analysis with Varimax rotation of 19 potential barriers that the authors identified as relevant to this population (Simons & Blount, 2007). The list of 19 barriers was a reduction from an initial 39 barriers. The 20 items that were eliminated were based on 90% or more of participants not endorsing the barrier as relevant, as well as one item dropped due to
item-total correlations. After the factor analysis was completed, four additional barriers were removed from the measure due to significant loading on other barriers. Within the remaining 16 barriers, there were four factor domains identified: “Disease Frustration/Adolescent Issues,” “Regimen Adaptation/Cognitive Issues,” “Ingestion Issues,” and “Parent Reminder.”

In order to examine construct validity, Simon and Blount (2007) did several correlations between subscales of the measure and demographic, disease, and family factors. There were no significant differences found based on age, developmental delay, gender, race, income, or parents’ educational background. There were also no differences found based on health care coverage, prescription drug coverage, or type of transplant. The less time that had elapsed since transplantation and the greater the number of medications the child was taking significantly correlated with higher scores on the subscale, “Ingestion Issues.” In addition, more frequent and intense side effects were correlated with higher scores on the subscale, “Disease Frustration/Adolescent Issues,” and total PMBS score. Using an analysis of variance, the authors found that the “Parent Reminder” subscale was significantly lower when the child and parent both agreed that the parent was primarily responsible for the child’s medication regimen. Additionally, higher scores on the “Parent Reminder” subscale were also associated with lower levels of child knowledge. When parent knowledge was lower, there were significantly higher scores on the subscales, “Disease Frustration/Adolescent Issues” and “Ingestion Issues.” While this measure has not yet been published in research beyond that of the original study, preliminary construct validity is promising.
In order to establish criterion validity, adherence was used as the standard to compare results from the measure. Simons and Blount (2007) used a self-report measure of adherence and an immunosuppressant drug assay to measure adherence. The authors categorized the patients into four groups based on results from both the self-report of adherence and the drug assay: “Genuinely Adherent,” “Deniers/Medically Complicated,” “At Risk,” and “Genuinely Nonadherent.” Both “Genuinely Adherent” and “Deniers/Medically Complicated” were considered to be adherent based on the self-report measure of adherence. A child was determined to be adherent when both the parent and the child reported that the child had ingested at least 90% of his or her medication over the past week. The “Genuinely Adherent” and “At Risk” groups were found to be adherent according to the drug assay level, meaning that the child’s medication levels were within the therapeutic range. The authors did not find a significant difference between the two adherent groups according to self-reported adherence: “Genuinely Adherent” and “Deniers/Medically Complicated.” There was also no significant difference between the two nonadherent groups according to self-report: “At Risk” and “Genuinely Nonadherent.” There were several differences detected between the adherent groups and nonadherent groups across all subscales, besides “Parent Reminder.” The “Deniers/Medically Complicated” group reported the fewest barriers and the “At Risk” group reported the most barriers. Among reports of the “Deniers/Medically Complicated” group and the two self-reported nonadherent groups significant differences were found in the total score, the “Disease Frustration/Adolescent Issues” subscale, and the “Regimen Adaptation/Cognitive Issues” subscale at the alpha level of \( p < .05 \). When the authors changed the criteria for significance to \( p < .10 \), then the total barriers and the subscales,
“Regimen Adaptation/Cognitive Issues” and “Ingestion Issues” were found to be significantly lower in the “Genuinely Adherent” group than in the “Genuinely Nonadherent” group. There were also significantly fewer items reported on the subscale, “Ingestion Issues,” in the “Genuinely Adherent” group versus the “At Risk” group at the alpha level of $p<.10$. Using adherence as the criterion to validate this measure, it was found that there were significant differences in the expected direction for the measure’s total score and subscale scores when comparing groups determined by adherence.

Adolescent Medication Barriers Scale (AMBS).

The Adolescent Medication Barriers Scale (AMBS) is a self-report measure used for adolescents to identify barriers to adhering to their medication regimen. It is a 5-point Likert-like scale ranging from “strongly disagree” to “strongly agree.” This measure was developed in conjunction with the PMBS in order to obtain a quantitative measure of barriers to adherence that adolescents face from their own perspective.

The AMBS was developed in much the same way as the PMBS, with only slight variations. For this measure, the authors began with 29 original items and reduced the number to a total of 17 items (Simons & Blount, 2007). The reasons for the decrease in items included: not being endorsed by enough children, item-total correlations, and loading on other barriers. After factor analysis with Varimax rotation, the final scale consisted of 17 total items. The AMBS consisted of only three subscales: “Disease Frustration/Adolescent Issues,” “Regimen Adaptation/Cognitive Issues,” and “Ingestion Issues.” Twelve of the items were the same as those in the PMBS with only slightly different wording. However, they did not all load on the same factors equally. Thus it is important to recognize that while the subscales on the PMBS and AMBS have the same
names, they do not represent the same items and are, therefore, not identical in the construct that is being captured.

Validity was determined for the AMBS in the same ways as for the PMBS. It had similar correlations between factors and subscales, indicating that the subscales are measuring what they are intending to measure. In addition, the authors measured the criterion validity by using the same four adherence groups as the PMBS. For the AMBS, there were also significant differences found between at least one of the self-reported adherent and nonadherent groups for all three subscales, as well as the total score. The validity of this measure is promising for use in children who have undergone solid organ transplantation.

The AMBS was developed for adolescents who have undergone solid organ transplantation. The primary reason both the AMBS and PMBS were developed was to quantitatively measure barriers to adherence in this population. Simons and Blount (2007) developed both of these measures with the child’s age range being from 11 to 21 years of age. A difference between the study that created the measure and the one presented here is that the age range was expanded to include children 7-years-old and above. Seven-year-olds have been found to be reliable sources of self-report (Riley, 2004) and neither the PMBS nor AMBS address barriers that would only pertain to children older than 11 years of age.

In order to determine the discrepancy score between the parent and child reports, the 12 items that were on both the PMBS and AMBS were used. First, both a child and parent discrepancy index score was calculated. This study used a methodology similar to that used by Christensen, Sullaway, and Margolin (1992) in a study looking at
discrepancies between mothers and fathers’ reports of children’s behaviors. The parent discrepancy index consisted of the number of items that the parent endorsed (i.e. responded either ‘Agree’ or ‘Strongly Agree’), but that the child did not endorse (i.e. responded either ‘Neutral,’ ‘Disagree,’ or ‘Strongly Disagree’). Conversely, the child discrepancy index consisted of the number of items that the child endorsed as a barrier, but that the parent did not endorse.

Statistical Analysis

The sample size in this study is consistent with much of the adherence literature, particularly studying this specific population. With the analyses that are used, in order to maintain a power of 0.80 while using an alpha level of .05, an effect size of .37 would be necessary to find significant results due to the sample size. Based on the statistic being calculated, an effect size of .37 is representative of a medium effect. It was believed that it would be feasible to obtain significant results with a medium effect size, as other studies using this population with similar sample sizes have found significant results. It is recognized that the degree of familywise error is somewhat high because all statistical analyses use an alpha level of .05 to determine significance. However, due to limitations of sample size, using this alpha level is justified given that this study is relatively novel and one of its primary purposes is to describe the importance of the relationship of parent and child report of barriers to adherence and to provide guidance for future research.

All three hypotheses were tested by calculating regression coefficients. A descriptive analysis was then conducted that examined each barrier and how parents versus children perceived the barrier. Child’s age has been found to be associated with
adherence (Dobbels et al., 2005). Therefore, the first step for all of the analyses was to calculate a Pearson’s correlation coefficient to determine if the child’s age was related to adherence in this sample. Since age was not found to be significantly related to adherence, a simple linear regression was calculated to test each of the primary hypotheses. An alpha level of .05 ($p < .05$) was used to determine if all calculated coefficients were significant.

In order to determine if number of barriers was predictive of adherence, simple linear regression coefficients were calculated. A regression coefficient was calculated for both child and parent report of the child’s barriers to adherence. Finally, a regression coefficient was calculated to determine if the discrepancy between parent and child report was predictive of adherence. In order to calculate the discrepancy scores, first a between-subjects t-test was used in order to determine if the child discrepancy index and the parent discrepancy index were significantly different from one another. This was done using the child group and the parent group as two independent groups and specific parent-child dyads were not paired for this portion of the analysis. Then, a regression coefficient was calculated for both the parent and child discrepancy scores to determine the extent to which the discrepancy scores are associated with adherence. Together these analyses indicated whether the child discrepancy score, the parent discrepancy score, or both discrepancy scores were significantly related to adherence. This allowed for an examination of the relationship between adherence and the discrepancy between parent and child perception of the child’s barriers, as well as the importance of whether it was the parent or the child who was endorsing more barriers when the other was not endorsing the barriers.
Due to limited sample size, it was not possible to do a complete statistical analysis of the item-by-item differences between parent and child report. Therefore, a descriptive analysis was conducted in order to guide future research on the topic.

Responses to each item that appears on both the PMBS and AMBS were entered into a parent-child agreement table. Table 2 shows an example of a parent-child agreement table and a separate one was made for each of the 12 items that appear on both the PMBS and AMBS. ‘Strongly Agree’ and ‘Agree’ were combined to be considered endorsing the item and ‘Strongly Disagree’ and ‘Disagree’ were combined to be considered not endorsing the item. ‘Neutral’ was considered separately from the other two categories. A percentage was calculated for each cell of the table. Once the tables were complete, the percentages of both parent and child agreeing (A), disagreeing (B), or being neutral (C) were summed to form a total percentage of agreement. The total percentage shows which items have higher and lower agreement between parent and child reports. This descriptive analysis provides information regarding which barriers were more highly endorsed by parents versus children, as well as which items they endorsed similarly.

Results

Adherence

Based on data obtained from the MEMS bottles, the average percentage of adherence over the monitored period for the children in this sample was 79.3%, with a standard deviation of 25.5%. Individual adherence percentages ranged from 0.0% to 100.0% adherence over the course of one month. The adherence percentage for each child was used in all of the following analyses as the outcome variable. The adherence
variable was examined for normality and determined to have a negatively skewed
distribution. Therefore, the variable was transformed using a reflect and logarithmic
transformation (Pallant, 2007). Analyses were run with both the original and transformed
data. Results reported below are based on the original data; but the transformed data also
produced no significant results.

Age.

In order to determine if age should be controlled for in the primary analyses, a
Pearson’s correlation coefficient was calculated to determine if age and adherence were
significantly related in the sample. It was found that age and adherence were not
significantly related in this sample ($r = -.23, p = .150$). Therefore, further analyses did not
control for age.

**Parent Medication Barriers Scale (PMBS).**

A simple linear regression was used to determine if the total score on the PMBS
was a predictor of adherence. It was hypothesized that an increased number of barriers on
the PMBS would predict poorer rates of adherence. However, this score was not found to
be a significant predictor of adherence, $F (1,39) = .015, p = .904$. Less than .001% of the
variance for adherence was accounted for by the total score of the PMBS ($R^2 = .001$).

**Adolescent Medication Barriers Scale (AMBS).**

A simple linear regression was used to determine if the total score on the AMBS
was a predictor of adherence. It was hypothesized that an increased number of barriers on
the AMBS would predict poorer rates of adherence. However, this score was not found to
be a significant predictor of adherence, $F (1,39) = .747, p = .393$. The variance for
adherence that can be accounted for by the total score of the AMBS was found to be 1.9% ($R^2 = .019$).

**Discrepancy between PMBS and AMBS.**

A between-subjects t-test was done to determine if there was a significant difference between the parent discrepancy index and the child discrepancy index. The results yielded insignificant results, indicating that there is no significant difference between the parent discrepancy index ($M = 1.76$, $SD = 1.68$) and the child discrepancy index ($M = 1.71$, $SD = 1.89$), $t(80) = -.123$, $p = .902$. A simple linear regression was then used to determine if either of the discrepancy index scores were a predictor of adherence. It was hypothesized that a larger discrepancy index would predict poorer rates of adherence for both the parent and child discrepancy index. The parent discrepancy index score was not found to be a significant predictor of adherence, $F (1,39) = .004$, $p = .950$. The parent discrepancy index score accounted for less than .001% of the variance for adherence ($R^2 = .001$). The child discrepancy index score was also not found to be a significant predictor of adherence, $F (1,39) = .138$, $p = .712$. The child discrepancy index score accounted for 0.4% of the variance for adherence ($R^2 = .004$).

Table 3 represents correlations between all measures that were administered, as well as data from the electronic monitoring bottles. There were no significant correlations between any measures or the electronic monitoring.

**Barriers to Adherence**

Although results of the primary analyses did not yield significant results, further qualitative analyses were computed in order to examine how often specific barriers were
reported. Barriers were considered ‘endorsed,’ ‘not endorsed,’ or ‘neutral’ based on responses of the PMBS and AMBS.

Table 4 represents the percentage of children who endorsed each of the barriers to adherence. Three barriers were endorsed by more than 25% of the children as being salient to them: “tired of living with a medical condition,” “tired of taking medication,” and “believing there are too many pills to take.” In addition, the table represents the percentage of children who endorsed the barrier when their caregivers did not also endorse that as a barrier for the child. There were three barriers that at least 20% of children endorsed but their caregivers did not also feel it was a barrier for the child: “tired of living with a medical condition,” “tired of taking medication,” and “dislike the way the medication tastes.”

Additionally, Table 4 represents the percentage of caregivers who endorsed each of the barriers to adherence that they felt their children experienced. Barriers to adherence that were endorsed by at least 25% of caregivers were: “tired of living with a medical condition,” “gets in the way of child’s activities,” and “tired of taking medication.” Two of these barriers were also of the top endorsed barriers by children, indicating that they are observed by both the child and parent. The table also represents the percentage of caregivers who endorsed a particular barrier when their children did not also endorse that as a barrier to adherence. One barrier was endorsed by at least 20% of caregivers whose child did not also consider it a barrier to adherence: “gets in the way of child’s activities.”

Finally, Table 4 shows the overall amount of agreement for each item between the child and caregiver. Agreement was defined as both the caregiver and child endorsing, not endorsing, or being neutral to the barrier. The barriers that had the highest level of
agreement (greater than 60%) between children and caregivers were: “hard time swallowing medication,” “not organized on how and when to take medication,” and “not wanting others to notice taking medication.” The barriers that had the lowest level of agreement (less than 40%) between children and caregivers were: “tired of living with a medical condition” and “gets in the way of child’s activities.”

**Discussion**

Archival data was used from a larger study researching individual and family variables that affect adherence in children who had undergone renal transplantation and their caregivers. The present study looked specifically at barriers to oral medication adherence, as perceived by both the child and parent. In addition to a quantitative measure of barriers to adherence, the study also monitored each child’s adherence over a 30-day period using electronic monitoring devices. Overall, rates of adherence were relatively high in the sample population compared to what would be expected. This population had an average rate of adherence of 79.3%, whereas the literature would suggest the average rate of adherence to be closer to 50.0% (Drotar, 2000; Osterberg & Blaschke, 2005; Rapoff, 1999). It is unclear why there was such a high rate of adherence; however, it could potentially be explained by other demographic factors of the population that participated in the study that were not examined in the present study, such as parents’ marital status (DiMatteo, 2004), socioeconomic status (Davis et al., 2001), or time since diagnosis (Rapoff, 1999). Furthermore, while average rates of adherence have been calculated across studies, specific studies have found highly variable rates of adherence (Dobbels et al., 2010). The overall higher rates of adherence from this sample population may have had some influence on the results, as it would be more challenging to find
significant differences since there was less variability among participants in terms of rates of adherence.

One demographic variable that the literature has found to frequently be related to adherence is age (Dobbels et al., 2005). Adolescents have been found to be less adherent as they are likely going through a process of increased autonomy and individualization (Rapoff, 1999). However, in the study population, age and adherence were not found to be significantly related. In fact, based upon the relatively high mean age, it might have been predicted that rates of adherence would be lower because adolescents are disproportionately represented. However, while age has been found to have a significant relationship with adherence, there are many other demographic factors that may play a role in adherence that were not considered in this study.

It was hypothesized that the number of perceived barriers to adherence would be related to the child’s adherence; however, this relationship was not found to be significant in this study. The measure that was used to capture barriers to adherence has been validated and determined to be a good predictor of a child’s adherence by the developers of the measure (Simons & Blount, 2007). However, the PMBS and AMBS have not been used in other published materials to date and the findings of this study did not replicate the findings of the original study. While this measure was not determined to be a predictor of adherence in this study, it is necessary to note that there were some differences between the study that was used to create the PMBS and AMBS and this one. The major differences include: type of transplant, sample size, age of participant, and definition of adherence. The sample size in the original study was larger than the sample size in this study; however, based on finding effect sizes that were close to zero, it is
suggested that the lack of relationship between number of barriers and adherence is more pressing than simply an issue of not having enough power to detect differences with this measure. Finally, the original study measured adherence with self-report and bioassay levels and then categorized children into one of four adherence groups. Although this is not an unusual way of measuring adherence, there was no real time monitoring. Based on the current literature that suggests that electronic monitoring is the best way to measure adherence (Quittner, Modi, Lemanek, levers-Landis, & Rapoff, 2007), the system that was used in the original study may account for some of the variability in findings or for the efficacy of this measure. Based on results from the current study, it would be suggested that while this measure does capture barriers to adherence from both the child and parents’ perspectives, it is not a good predictor of adherence. Therefore, it is necessary to look further into specific barriers to adherence, and what they might mean for the families who are experiencing them.

One factor that may affect barriers to adherence that is not addressed in the PMBS or AMBS is the influence that timing may have on the results. The measure does not have a defined timeframe (i.e. within the past month) so it is impossible to know what period of time is being captured by participants’ responses. This may be particularly important when including children with wide variability in the time that has elapsed since their transplant or initial diagnosis. The amount of time that has passed since their transplant can impact the types of numbers of barriers to adherence, as well as adherence rates (Rapoff, 1999). If the measure defined the time in which it was capturing, it would give insight into barriers that affect children at different times by asking only about current
barriers to adherence. By not recognizing the importance of capturing specific time points, an important component of barriers to adherence may have been missed.

Beyond the potential limitations of the measure, the fact that the number of barriers to adherence was not a predictor of adherence requires additional inquiry as to its meaning. Previous studies have found mixed results on the predictive power of barriers to adherence on adherence outcomes (Marhefka et al., 2008; Modi & Quittner, 2006; Simons, McCormick, Mee & Blount, 2009; Steele et al., 2001; Zelikovsry, Schast, Palmer, & Meyer, 2008), which leads to the possible conclusion that studying barriers to adherence alone is not sufficient in understanding what truly predicts adherence outcomes. Although participants are experiencing challenges to taking medication, they do not appear to be large enough to prevent them from taking it. However, there are also families in this study that are not endorsing many barriers to adherence, yet for some reason the child is not taking the medication consistently. This is a more difficult group of families to understand, yet the ones who would likely benefit the most from intervention. Does the measure not adequately reflect the barriers that these children are experiencing? Do families not perceive specific barriers despite the fact that they are present? Do they not understand the medication regimen or the importance of adherence?

All of these questions, and many more need to be considered when working with families who are not perceiving common barriers to adherence, despite the clear evidence that they are not following through with medical advice. The results from this study suggest that it is more important to understand what is getting in the way of a family’s adherence than the sheer number and intensity of the barriers, as reported by either the parent or the child.
Another important point to consider when examining the research on barriers to adherence is the way that barriers are measured and defined. Studies vary widely on the ways that barriers are measured and defined, with several using more of an interview-based qualitative design (Modi & Quittner, 2006; Steele et al., 2001). When quantitative designs are used, authors frequently choose and combine measures that were created for purposes other than examining barriers to adherence. Therefore, despite the fact that quantitative measures are sometimes being used, the authors are still subjectively choosing which measures best represent the way that barriers to adherence are defined. This leads to the question of what is really being studied when authors use the terminology of barriers to adherence. It is more than a single domain, despite the way that it is sometimes discussed in the literature. The variability across studies makes it particularly difficult to determine if barriers to adherence can predict adherence outcomes. Disease-specific measures are beginning to be developed that are focusing specifically on the topic of barriers to adherence; however, they are still early in development and may need additional modifications. Another limitation to researching barriers to adherence is the usage of both parent and child report of perceived barriers. It is best to consider data from both parent and child perspectives (Varni, Jacobs, & Seid, 2000); however, it is difficult to know if similarities and differences are rooted in true differences in perceptions or in differences in reporting. This is not a limitation unique to adherence research; however, it is one that needs to be considered when examining the findings of this study.

Another reason research focusing on barriers to adherence does not have consistent findings may be that some researchers look strictly at the number of barriers
endorsed. This method does not capture the intensity of the impact of a single barrier on a person. For example, one patient may have three barriers which only place a small burden on him, while another patient may have one barrier that is strongly prohibitive to her taking her medication. The factors involved with studying barriers to adherence point to the significance of continued research in the field of barriers to adherence.

To further explore the importance of the parent versus the child’s report of barriers, each of these reports was broken down further. Although neither were a predictor of adherence, the specific barriers were examined qualitatively. Both parents and children considered being “tired of taking medication” and “tired of living with a medical condition” to be among the biggest barriers for adherence. However, they were among the lowest in terms of agreement between the parent and child. This means that individually many parents and children see these barriers as problematic, but parent-child dyads are often not both seeing them as problematic. The barriers for which parents and children had higher levels of agreement included more concrete barriers such as having a “hard time swallowing medications” and “not being organized.” This is not surprising as parents and children have been found to have higher rates of agreement on behaviors that are more overt (Verhey et al., 2009). However, while they are seeing these barriers in the same ways, they are typically in agreement that these are not barriers to adherence for the child. The analysis indicates that concerns that are more internal to the child, such as being “tired of taking medication” or “believing there are too many pills to take” may be useful to address in interventions, due to their high frequency but low agreement rate. The disagreement between parents and children indicates that both should be involved in the therapeutic process when working on difficulties for adherence, as the experience is
not the same for both of them and it would be anticipated that the involvement of both the parents and children is necessary for optimal improvement.

Additionally, in order to address the fact that researchers are not finding consistent results with focusing on barriers to adherence for the child, it may be useful to shift the focus to barriers to adherence for the parent. The findings from this study indicate that the number of barriers to adherence that the child experiences is not related to adherence outcomes. However, when working with children and adolescents the parents’ approach to adherence is possibly more important to the final outcomes (Conn, Halterman, Fisher, Yoos, Chin, & Szilagyi, 2005). It may be that the barriers that interfere with the parent’s ability to get the child to take the medication are truly what impact the child’s overall adherence. Future research should consider examining parents’ perceptions of their own barriers, rather than the barriers of their children, as these may play a much larger role in the final outcome of whether or not the child adheres to his or her treatment regimen.

Although many have already been discussed throughout this section, there are additional limitations to this study. The present study was done at a single site with a relatively small sample size. Continued exploration of barriers to adherence and their effect on adherence outcomes should be done with a wider range of families and a larger sample. In addition, adherence was only monitored for 30-days, which gives only a small sample of the child’s overall adherence behavior. The MEMS bottle also only monitored one medication that the child was prescribed, which for many children is only a small percentage of their overall regimen. Finally, the children widely varied in the amount of
time that had passed since their transplant. This may have affected the number and types of barriers experienced, as well as the child’s adherence.
References


epilepsy: What is the level of agreement between youth and their parents?

_Epilepsy & Behavior, 14_, 407-410.

Table 1

*Demographic Information*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean ± SD</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s Age</td>
<td>15.0 ± 3.0 years</td>
<td></td>
</tr>
<tr>
<td>Child’s Sex</td>
<td></td>
<td>Female = 41.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male = 58.5</td>
</tr>
<tr>
<td>Child’s Race</td>
<td></td>
<td>Caucasian = 78.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>African American = 22.0</td>
</tr>
<tr>
<td>Time Since Transplant</td>
<td>4.5 ± 3.7 years</td>
<td></td>
</tr>
<tr>
<td>Annual Family Income</td>
<td></td>
<td>&lt;$10,000 = 2.4</td>
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<tr>
<td></td>
<td></td>
<td>$10,000-$19,999 = 9.8</td>
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<tr>
<td></td>
<td></td>
<td>$20,000-$29,999 = 7.3</td>
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<td></td>
<td></td>
<td>$30,000-$39,999 = 4.9</td>
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<td>$40,000-$49,999 = 12.2</td>
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<td></td>
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<td>$50,000-$59,999 = 4.9</td>
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<td></td>
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<td></td>
<td></td>
<td>$80,000-$89,999 = 9.8</td>
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<td></td>
<td></td>
<td>$90,000-$99,999 = 9.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥$100,000 = 14.6</td>
</tr>
<tr>
<td>Respondent’s Relationship</td>
<td></td>
<td>Mother = 78.0</td>
</tr>
<tr>
<td>to Child</td>
<td></td>
<td>Father = 9.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grandmother = 9.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other = 2.4</td>
</tr>
<tr>
<td>Respondent’s Marital Status</td>
<td></td>
<td>Married = 68.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single = 7.3</td>
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<td></td>
<td></td>
<td>Separated = 7.3</td>
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<td></td>
<td></td>
<td>Living as Married = 7.3</td>
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<tr>
<td></td>
<td></td>
<td>Divorced = 4.9</td>
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<td></td>
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<td>Widowed = 4.9</td>
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Table 2

*Parent-Child Agreement Table*

<table>
<thead>
<tr>
<th>Item 1</th>
<th>Agree</th>
<th>Disagree</th>
<th>Neutral</th>
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</thead>
<tbody>
<tr>
<td>Agree</td>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disagree</td>
<td></td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td></td>
<td></td>
<td>C</td>
</tr>
</tbody>
</table>

*Note.* Total agreement score = A+B+C
Table 3

*Correlations Between Variables Measured*

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Percent Adherence</th>
<th>PMBS Score</th>
<th>AMBS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>---</td>
<td>-0.23</td>
<td>-0.02</td>
<td>-0.08</td>
</tr>
<tr>
<td>Percent Adherence</td>
<td>-0.23</td>
<td>---</td>
<td>0.02</td>
<td>-0.14</td>
</tr>
<tr>
<td>PMBS Score</td>
<td>-0.02</td>
<td>0.02</td>
<td>---</td>
<td>0.13</td>
</tr>
<tr>
<td>AMBS Score</td>
<td>-0.08</td>
<td>-0.14</td>
<td>0.13</td>
<td>---</td>
</tr>
<tr>
<td>Barrier</td>
<td>Endorsed by Child (%)</td>
<td>Endorsed by Child Only&lt;sup&gt;a&lt;/sup&gt; (%)</td>
<td>Endorsed by Caregiver (%)</td>
<td>Endorsed by Caregiver Only&lt;sup&gt;b&lt;/sup&gt; (%)</td>
</tr>
<tr>
<td>--------------------------------------------------------------</td>
<td>-----------------------</td>
<td>---------------------------------------</td>
<td>---------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Tired of taking medication</td>
<td>41.5</td>
<td>26.8</td>
<td>26.8</td>
<td>12.2</td>
</tr>
<tr>
<td>Tired of living with a medical condition</td>
<td>41.0</td>
<td>26.8</td>
<td>33.3</td>
<td>19.5</td>
</tr>
<tr>
<td>Believes too many pills to take</td>
<td>29.3</td>
<td>19.5</td>
<td>17.1</td>
<td>7.3</td>
</tr>
<tr>
<td>Gets in the way of activities</td>
<td>24.4</td>
<td>19.5</td>
<td>26.8</td>
<td>22.0</td>
</tr>
<tr>
<td>Does not like how the medicine tastes</td>
<td>22.5</td>
<td>23.3</td>
<td>15.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Does not want others to notice taking medication</td>
<td>19.5</td>
<td>12.2</td>
<td>17.1</td>
<td>9.8</td>
</tr>
<tr>
<td>Forgets/Doesn’t remember to take medication every time</td>
<td>19.5</td>
<td>7.3</td>
<td>24.4</td>
<td>12.2</td>
</tr>
<tr>
<td>Not very organized about when and how to take the medication</td>
<td>14.6</td>
<td>7.3</td>
<td>14.6</td>
<td>7.3</td>
</tr>
<tr>
<td>Doesn’t like effect on appearance</td>
<td>12.2</td>
<td>7.3</td>
<td>17.1</td>
<td>12.2</td>
</tr>
<tr>
<td>Too hard to stick to a fixed medication schedule</td>
<td>9.8</td>
<td>7.3</td>
<td>14.6</td>
<td>12.3</td>
</tr>
<tr>
<td>Believes medication has too many side effects</td>
<td>7.5</td>
<td>7.5</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Hard time swallowing medication</td>
<td>4.9</td>
<td>4.9</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

\[a\] Child endorsed the barrier to adherence, however, the caregiver did not also endorse that it is a barrier to adherence for the child

\[b\] Caregiver endorsed the barrier to adherence, however, the child did not also endorse that it is a barrier to adherence for the child

\[c\] Total percentage of children and parents who agree that the barrier either is or is not a barrier or that they are neutral to whether or not it is a barrier
30 July 2010

Ms. Lauren Perazzo
30 E. Central Parkway #202
Cincinnati, OH 45202

Re: Protocol #1015: Barriers to Medication Adherence Following Pediatric Renal Transplantation: The Utility of Independent and Interrelated Parent and Child Reports

Dear Ms. Perazzo:

The IRB has reviewed the materials regarding your study, referenced above, and has determined that it meets the criteria for the Exempt from Review category under Federal Regulation 45CFR46.101(b)(4). Your protocol is approved as exempt research, and therefore requires no further oversight by the IRB. In granting this approval, we assume that the PI of the original study has met all necessary obligations to the CCHMC IRB in granting permission to you to create the fully de-identified data file and use these anonymous, archival data.

If you wish to modify your study, it will be necessary to obtain IRB approval prior to implementing the modification. If any adverse events occur, please notify the IRB immediately.

Please contact our office if you have any questions. We wish you success with your project!

Sincerely,

Sincerely,

[Signature]

Morell E. Mullins, Jr., Ph.D.
Chair, Institutional Review Board
Xavier University

CC: Janet Schultz, advisor
Appendix B

The Parent Medication Barriers Scale (PMBS) is protected by copyright so it is not reproduced in this document. The measure is available by contacting the developing author, Laura E. Simons, at laura.simons@childrens.harvard.edu.
Appendix C

The Adolescent Medication Barriers Scale (AMBS) is protected by copyright so it is not reproduced in this document. The measure is available by contacting the developing author, Laura E. Simons, at laura.simons@childrens.harvard.edu.
Barriers to Medication Adherence Following Pediatric Renal Transplantation:

The Utility of Independent and Interrelated Parent and Child Reports

Problem

In the past fifty years, advancements in immunosuppressant medication have allowed transplantation to become a viable treatment option for children with end-stage-renal-disease (ESRD) (Hatch & Agrawal, 2009). Transplantation has substantially increased the long-term survival of children with ESRD but the oral medication regimen that follows transplant requires ongoing management. Adherence to the immunosuppressant medication regimen is difficult. However, high levels of adherence are essential for optimal health outcomes since advances in medicine are only as beneficial as the extent to which the patient follows through with his or her treatment regimen.

Despite known negative health outcomes (Shaw, Palmer, Blasey, & Sarwal, 2003), average rates of nonadherence in pediatric renal transplant recipients have been found to be approximately 32%, with some studies finding rates of nonadherence as high as 75% (Dobbels, Damme-Lombaert, Vanhaecke, & De Geest, 2005; Dobbels, Ruppar, DeGeest, Decorte, Damme-Lombaerts, & Fine, 2010). Although literature exists about the importance of adherence, specific barriers to adherence are not well established in this population. Similarly, research is conflicted on the importance of reducing the number of barriers (Modi & Quittner, 2006; Simons, McCormick, Mee, & Blount, 2009; Steele, Anderson, Rindel, Dreyer, Perrin, Christensen et al., 2001; Zelikovsky, Schast, Palmer, & Meyer, 2008). A better understanding of the relationship between the number of barriers for the child and adherence would help to identify patients at risk for poorer adherence.
For children and adolescents, achieving adherence is not a task that is only relevant for the child. When a child has a chronic illness, the entire family is typically involved in the management of the regimen (Beveridge, Berg, Wiebe, & Palmer, 2005). Reports from both the parent and child’s perceptions of the barriers that the child faces to adherence allow for a more thorough assessment and formation of effective interventions to address barriers to adherence.

Method

Archival data from 41 children and their caregivers were used to determine if there was a relationship between the number of barriers to adherence and child’s adherence to oral medication. Data were used from the Adolescent Medication Barriers Scale (AMBS) and the Parent Medication Barriers Scale (PMBS) in order to obtain the number of barriers that each child faced to adherence. Additionally, data were available for the child’s adherence to immunosuppressant medication, which was measured using an electronic monitoring device (MEMS) over a 30-day period.

It was hypothesized that the greater the number of barriers to adherence, the lower the child’s adherence would be based on results from both the AMBS and the PMBS. In addition, it was hypothesized that the greater the discrepancy between the AMBS and the PMBS, the lower the child’s overall adherence would be.

Findings

Based on the predetermined sample size, it was determined that an effect size of .37 would be necessary to find significant results. This is representative of a medium effect size. The average rate of adherence in this sample was 79.6% over the 30-day
period. Regression coefficients were used to conduct the analyses for the three primary hypotheses. None of the regression coefficients yielded significant results.

An additional qualitative analysis was done to look at specific barriers to adherence from both the child and the parent's perspective. The three barriers that were most frequently endorsed by the child included: tired of living with a medical condition, tired of taking medication, and believing there are too many pills to take. The three barriers that were most frequently endorsed by the parent included: tired of living with a medical condition, gets in the way of activities, and tired of taking medication. In order to get a better understanding of how barriers are perceived by the family system, barriers that were endorsed by one party and not endorsed by the other were also examined. It was found that there were three barriers that at least 20% of children endorsed when their caregivers did not also feel it was a barrier for the child: tired of living with a medical condition, tired of taking medication, and dislike the way the medication tastes. One barrier was endorsed by at least 20% of caregivers whose child did not also consider it a barrier to adherence: gets in the way of his/her activities. Overall, the highest rates (>60%) of agreement were: hard time swallowing medication, not organized on how and when to take medication, and not wanting others to notice taking medication. The lowest rates (<40%) of agreement were tired of living with a medical condition and gets in the way of activities.

Implications

Results from the primary hypotheses indicate that the number of barriers that a child experiences was not predictive of the child's adherence. This was true from both the perspectives of the child and the parent. In addition, the discrepancy between the parent
and the child’s report was not predictive of the child’s adherence. Therefore, it can be concluded that looking purely at the number of barriers to adherence is not a good way to predict whether or not the child will have higher adherence rates. This implies that additional exploration is necessary to determine what gets in the way of adherence for the child.

Using the measures that were given in this study, specific barriers to adherence can be identified from both the child and the parent’s perspectives. Barriers that are more difficult for the caregiver to see, such as being tired of taking medication and living with a medical condition were the most highly endorsed by both children and their parents. On the other hand, strictly behavioral barriers, such as difficulties swallowing pills or organization were not endorsed as highly. Interventions surrounding barriers to adherence should focus on the specific barriers to adherence from both the parent and child based on the fact that they see some things similarly, but also present with some variability. Additionally, interventions should include both the external and internal struggles of living with a chronic illness. Finally, additional research is needed to better understand how barriers to adherence affect adherence outcomes and which barriers should be the focus of interventions.