

**Pediatric Kidney Transplantation: Identifying and Addressing Post-Transplant Barriers to Adherence Through an Integrated Healthcare Approach**

by

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**Abstract**

Medical non-adherence represents a significant challenge in health care treatment, and has demonstrated taxing effects on health outcomes and overall healthcare expenditures. UPMC Children’s Hospital of Pittsburgh serves a diverse population of pediatric kidney transplant patients, many of whom are deemed “high-risk” transplants, with high-risk encompassing various biopsychosocial components. A retrospective chart review demonstrated that many patients deemed low-psychosocial risk prior to transplant had higher rates of rejection in the first three years post-transplant, suggesting a need to implement post-transplant screenings assessing non-adherence and the continued involvement of a multidisciplinary medical team after transplant. Utilizing a socioecological lens, a multitude of factors were assessed by the CHP kidney transplant team as being relevant to patient adherence including social determinants of health, psychological functioning, and related adherence variables. The team developed the novel protocol highlighted in this paper in order to ensure access to the psychosocial team while identifying and addressing barriers to adherence in a standardized manner with collaboration across the interdisciplinary medical team. Kidney transplant patients followed at CHP and their parents/guardians completed a collection of measures as a component of this novel systematic protocol implemented in an integrated delivery system. Of the 148 eligible for annual post-transplant evaluations, the team completed annual evaluations on 82 patients and parents/guardians if applicable. Exclusion criteria

was applied, and reasons for non-completion were coded appropriately and subsequently assessed. The data collected in year one and pilot program changes are used to assess overall reach, completion of data, themes of non-adherence, and the feasibility of a UPMC Quality Improvement project. These results can be used to inform future holistic assessments, protocols, medical practices, and potential for long-term implications while continuing these study aims prospectively. Public health significance pertains directly to the associated social determinants of health and subsequent implications on health systems and applicable policies.

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## 1.0 Introduction

Solid organ transplantation represents a significant transformation in healthcare, markedly altering the course of survival and quality of life for those with end-organ dysfunction. Solid organ transplantation includes liver, kidney, heart, lung, and/or pancreas with kidney transplant rates exceeding all other categories, arguably due to the donor level status (e.g., deceased and/or living donation) possible with this specific organ (Black, Termanini, Aguirre, Hawksworth, & Sosin, 2018). According to the U.S. Department of Health and Human Services Organ Procurement and Transplantation Network, national rates of overall kidney transplantation and pediatric kidney transplantation have increased each year. In 2019, medical teams across the nation completed 760 pediatric (<18 years old) kidney transplants out of 23,401 kidney transplants across all ages. Comparing these statistics to all organ data highlights the substantial kidney transplant rates, where 39,718 total solid transplants were completed in 2019 and 1,923 of those on pediatric patients (U.S. Department of Health and Human Services: HRSA, 2020).

Medical non-adherence and non-compliance represent significant challenges in health care treatment, particularly regarding the increasing complexity of medical treatment regimens related to organ transplantation. Non-adherence factors have taxing implications on graft loss related to solid organ transplantation, overall health outcomes across many chronic conditions, and costly healthcare expenditures. As highlighted in this paper, many contributing factors and barriers to adherence are products of social determinants of health, specifically relating to transplant recipients navigating life-long complex medical regimens post-transplant.

As many world-renowned transplant centers in the US complete holistic pre-transplant assessments to identify modifiable risk factors and potential barriers to adherence, these processes

could be translated to post-transplant care as part of the care received at these integrated delivery systems. UPMC Children's Hospital of Pittsburgh (CHP) Pediatric Kidney Transplant Team initiated a pilot program seeking to improve adherence by identifying and addressing various barriers to adherence. Through this novel program's implementation, the team aimed to address gaps in care, identify barriers to adherence, effectively address these barriers, and improve overall health outcomes for pediatric kidney transplant patients.

## **2.0 Background**

### **2.1 Literature Background**

Medical professionals often use the terms compliance and adherence interchangeably, although these terms at times have different connotations. Adherence is often defined as the extent to which patients follow prescribed treatment (Hugtenburg, Timmers, Elders, Vervloet, & Dijk, 2013). The Mayo Clinic posits that adherence suggests patient agreement and compliance insinuates patient passivity (Brown & Bussell, 2011). The University of Cincinnati Transplant Clinical research supports similar sentiments, but includes behavioral processes influenced by multiple domains. They denote five main domains of adherence: health system factors, social and economic factors, condition-related factors, therapy-related factors, and patient-related factors (Alloway, n.d.). Adherence has replaced compliance in many settings as it emphasizes clinician-patient relationship while often considering the patient's health beliefs, circumstances, and available resources. The nature of compliance puts all responsibility on the patient and often corresponds with a negative label. Alternatively, adherence emphasizes the patient's voice in the process and places responsibility on the collaborative care relationship. Medical teams have worked to shift the language from compliance to adherence, as is reflected through the work of CHP.

While primarily connected to prescription medication adherence, medical teams apply the term to other suggested treatment areas, such as appointment attendance, dietary intake, lifestyle factors, and following other recommendations from practitioners. Regarding medication adherence specifically, 50% of those with chronic illnesses do not take their medications as

prescribed (Brown & Bussell, 2011). The World Health Organization emphasizes the importance of expanding the adherence term to encompass multiple facets of care including therapeutic health behaviors such as filling prescriptions, self-management factors (e.g., smoking, contraception, risky sexual behaviors, unhealthy diet, and physical activity levels), obtaining immunizations, and maintaining the quality care relationship between patient and provider (World Health Organization, 2003).

Medical non-adherence represents a taxing and costly component in the healthcare system. Morbidity and mortality are increased exponentially by non-adherence, and suggested financial costs are estimated to exceed \$100 billion per year (Brown & Bussell, 2011). Non-adherence has also been associated with over-utilization of health services and subsequent healthcare system waste (Zelikovsky, Schast, Palmer, & Meyers, 2008). The Johns Hopkins School of Public Health in collaboration with the Johns Hopkins School of Medicine and Community Physicians completed a brief analysis on health care costs related to adherence. Their report emphasized the critical nature of considering non-adherence as an important public health topic due to the direct effects on health outcomes and costs. Between 20% and 30% of the trillions of dollars spent on healthcare in the United States have been determined to be wasteful. Patient non-adherence directly contributes to this costly amount, with an estimated burden of billions each year from arguably avoidable costs. In order to properly address non-adherence, healthcare professionals must increase their understanding of factors affecting adherence. Strategies should be applied to increase adherence, including those targeting patient, provider, and external determinants (Iuga & McGuire, 2014).

Overall, fragmented healthcare systems have created and exacerbated barriers to adherence by restraining effective care coordination and overall access to care (Brown & Bussell, 2011).

Many contributing factors are influenced by social determinants of health. The Mayo Clinic highlights three main areas of contributing factors to non-adherence: patient related (e.g. low health literacy, behavioral health components, financial means, and support), physician related (e.g. prescription of complicated treatments, ineffective communication, inclusion of multiple physicians, and barriers to communication), and overall healthcare systems (e.g. limited visit times, lack of access, and insurance factors). Because of this multifaceted complexity, solutions to address non-adherence should be comprehensive and interdisciplinary in nature to match the inherent intricacy (Brown & Bussell, 2011). Overall, healthcare professionals have increasingly drawn attention to addressing social determinants of health through the integrated care of patients, yet research on addressing these variables as they involve barriers to adherence is limited, particularly relating to the care of pediatric patients.

Specifically related to transplant populations, the Scientific Registry of Transplant Recipients (SRTR) consistently tracks and publishes outcomes regarding all solid organ transplants, with the hopes of providing a platform where patients and families can make informed decisions regarding their preferred transplant centers. Their mission is “to provide advanced statistical and epidemiological analyses related to solid organ allocation and transplantation in support of the Department of Health and Human Services and its agents in their oversight of the national organ transplantation system” (Scientific Registry of Transplant Recipients, 2020). Furthermore, they track patients and publish outcomes for the one-year and three-year marks post-transplant regarding graft function, mortality, hazard ratios, and multiple aspects of care. Graft loss and mortality directly impact each center’s scores and highlighted outcomes in this internationally accessible database (Scientific Registry of Transplant Recipients, 2020). Combining these statistics with research highlighting the direct impact of non-adherence on health outcomes,

hospitals should recognize the financial and status incentives to incorporate programs aimed at addressing non-adherence factors that can directly impact post-transplant outcomes.

Current interventions targeting medication non-adherence in various patient populations suggest overall ineffectiveness. One review suggested that previously utilized interventions reduced medication non-adherence only half of the time, caused little change in treatment outcomes, and overall showed a modest change effect. The same report highlighted that these interventions were targeted broadly at every patient regardless of non-adherence levels and were not individualized to address individual patient needs (Hugtenburg et al., 2013). The authors suggest an urgent need for specific approaches based on each individual and circumstances surrounding their non-adherence. Furthermore, most published reports rely on retrospective observational designs, thus impeding the ability to suggest direct links between changes in adherence and effects on health care costs and outcomes.

In recent years, researchers have studied the existence of non-adherence in transplant patients, as post-transplant care often involves significant adjustments and life-time management of medications, treatments, developmental concerns, symptom monitoring, and follow-up/lab appointments. Pediatric transplant patients and their families often face numerous challenges in navigating post-transplant care, yet research is limited relating to this specific population. Numerous gaps in the literature exist in addition to a lack of standardized approaches currently in practice across the national healthcare system.

Many psychosocial aspects and social determinants of health relate to post-transplant functioning and outcomes, with a direct relationship between medication non-adherence and organ rejection. This suggests an inarguable direct impact on health outcomes. Renal transplant patients with immunosuppression medication non-adherence have increased rates of graft loss, which can

lead to the patient “losing” their transplanted organ, thus returning to their pre-transplant state. Consequently, this can lead to the need for dialysis, re-transplantation, and/or mortality. Graft loss, or loss of function in the transplanted kidney, is often measured by graft survival rates. According to the Organ Procurement and Transplantation Network/United Network of Organ Sharing, roughly 30% of kidney recipients experience graft loss or mortality within five-years. Although explanations for graft loss can pertain to medical markers such as a nonviable transplanted organ, technical issues, and acute rejection, non-adherence affects graft survival particularly related to medication adherence of immunosuppressants and other pertinent prescribed pharmaceuticals. Medical teams emphasize the maintenance of immunosuppressant medications to preserve renal function, hinder rising panel reactive bodies, and prevent allograft loss (Marcen & Teruel, 2008). Despite these factors, non-adherence among renal transplant patients can range between 20%-70%. These same researchers suggested associations between non-adherence and psychosocial factors such as depression, self-efficacy, problem solving skills, health beliefs, social support, the existence of an external locus of control, and overall neurocognitive abilities (Paterson, O’Rourke, Shapiro, & Thornton, 2018).

Many health centers implement rigorous, all-encompassing pre-transplant psychosocial assessments, yet lack established protocol for post-transplant screening initiatives. The Children’s Hospital of Philadelphia emphasizes the importance of identifying barriers with potential transplant patients during the listing phase in order to apply early intervention for proper preparation. Using the Medical Adherence Measure, their results suggested that the more barriers pediatric renal transplant candidates perceived, the greater likelihood of missed medication doses and/or late doses. Calculating adherence as percent of self-reported missed doses, 89.1% of participants displayed markers of non-adherence (i.e. missed or late medication doses).



Acknowledging the unrealistic nature of perfect adherence, they applied a lenient cut-off of greater than or equal to 10% of missed doses. With this adjustment, 38.2% of adolescents were listed as non-adherent. While medical practitioners emphasize the importance of timely consumption of immunosuppression medications, 23.6% of adolescents reported late doses. Researchers also highlighted the importance of parental involvement, as independent management was a key perceived barrier. Other modifiable barriers included lack of knowledge regarding the medication regimen, lack of organization systems in place such as a pillbox, forgetfulness, believing the regimen interfered with activities, and a dislike of the taste. Although the study did not test specific interventions, they highlighted numerous perceived barriers to adherence in a standardized manner via established questionnaires (Zelikovsky et al., 2008).

A Duke University School of Medicine retrospective analysis highlighted the importance of determining risk of pre-transplant pediatric renal patients via standardized psychosocial assessments. They utilized the Psychosocial Assessment of Candidates for Transplantation (PACT) to recognize those at risk for adverse clinical outcomes after renal transplant based on a scale ranging from poor candidate to excellent candidate. In combination with demographics and clinical outcomes, social workers utilized PACT to assess transplant candidates in four domains: social support, psychological health, lifestyle factors, and understanding. Out of 54 pediatric patients, the medical team completed PACT assessments on 25 patients. Those evaluated with PACT had notably lower percentages of acute organ rejection and non-adherence. Their results suggest that a lack of family availability/support, risk for psychopathology, and unstable personality factors were associated with lower medical adherence. Overall, Duke's pilot study suggested the effectiveness of standardized evaluation using PACT by highlighting modest improvements in clinical outcomes (Freischlag et al., 2019).

Researchers at the Epidemiology and Clinical Research of the Johns Hopkins Medical Institutions completed a prospective observational cohort study of 13 pediatric kidney transplant recipients and their caregivers. They aimed to assess the potential impact of modifiable psychosocial aspects on adherence to prescribed medication measures via standardized questionnaires. Caregivers completed behavioral and attitudinal surveys, and patients completed these if they were literate. Researchers calculated medication adherence ratios, and board-certified pediatric nephrologists (kidney specialists) assessed immunosuppressant lab values in order to categorize patients and families as ‘probably adherent (PA)’ or ‘possibly non-adherent (PNA).’ They used Pearson correlation coefficients and t-tests to assess potential associations between adherence and psychosocial variables. Their results suggested an association between poor medication adherence and the following variables: higher parental stress, child behavior issues, increased dissatisfaction with body image, and dysfunctional parent-child interactions. Despite the small sample size, their research provides preliminary support for the relationship between psychosocial factors and non-adherence in pediatric renal transplant recipients (Gerson, 2004).

A 2008 meta-analysis reported the majority of healthcare organizations that institute non-adherence protocol with transplant populations use limited domains (i.e., various aspects of the care regimen), and often rely on immunosuppressant medication as the sole domain in assessing non-adherence. When targeting pediatric specific studies, they found that psychosocial factors demonstrated the strongest relationship with the non-adherence variable. Although the authors deemed this as “encouraging” as these psychosocial factors are modifiable with targeted interventions, many centers still lack adequate targeted approaches for addressing these factors (Kahana, Frazier, & Drotar, 2008). Alternatively, the Division of Transplant Surgery at the Medical University of South Carolina assessed if appointment non-adherence was both correlated

with medication non-adherence, and served as a predictor for graft loss. Utilizing a longitudinal cohort study, their results suggest a strong correlation between appointment non-adherence and medication non-adherence. Patients with appointment non-adherence were at a 1.5 times higher risk of acute rejection episodes (22.0% vs. 14.7%,  $p < 0.0001$ ), and a 65% higher risk of overall graft loss (95% CI 1.38–1.97,  $p < 0.0001$ ). Those with both medication and appointment non-adherence were at an even higher risk of graft loss. Overall, their results suggest that non-adherence factors of various domains can impact transplant outcomes and correlate with one another (Taber et al., 2017).

In general, across the national healthcare sector, current solid organ transplantation lacks standardized tools and programs in completing pre-transplant psychosocial evaluations, and these deficits often translate to subsequent gaps in post-transplant evaluations. Many established measures studied in adult transplant patients have not been studied in pediatric solid organ transplant programs suggesting a need for translation to pediatric patients and caregivers (Freischlag et al., 2019). In order to advance the continuum of care, decrease medical waste, maintain transplant center status, and holistically address non-adherence, centers should address post-transplant biopsychosocial risk with all-encompassing psychosocial assessments adapted to their respective patient populations.

## **2.2 UPMC Children’s Hospital of Pittsburgh Background**

The University of Pittsburgh Medical Center (UPMC) Children's Hospital of Pittsburgh (CHP) serves a diverse population of pediatric kidney transplant patients, many of whom are deemed “high-risk” transplants. High risk can encompass multiple facets of care including medical

and psychosocial components. The integrated transplant team (consisting of nephrologists, transplant surgeons, nurse coordinators, transplant psychology, transplant social work, dietary, and pharmacy) has historically completed extensive pre-transplant assessments in order to prepare families for transplant while seeking modifiable potential barriers to adherence. However, like many other pediatric centers, they have historically lacked systematic post-transplant evaluations and continue to face challenges related to non-adherence. CHP transplant services define adherence as following all aspects of a medical regimen (medication and dietary requirements), attendance of scheduled appointments, and continual communication between the patient and medical team. They acknowledge the unrealistic nature of perfect adherence, and that patients may have instances of non-adherence throughout their transplant journey. Nonetheless, the pattern of non-adherence puts one at greater risk of adverse health outcomes following transplant. The integrated transplant team recognizes that multiple factors impact adherence such as health beliefs, poor understanding, mental health diagnoses, socioeconomic status, education, cultural and religious beliefs, and the existence of social support structures (UPMC Children's Hospital of Pittsburgh, 2020).

A retrospective chart review completed by the Transplant Psychologist and Kidney Transplant Medical Director at CHP demonstrated that many patients deemed low-psychosocial risk prior to transplant had higher rates of rejection in the first three years post-transplant, suggesting a need to implement post-transplant screenings and include the continued involvement of a multidisciplinary medical team after transplant. Those deemed high risk prior to transplant had a greater presence of the medical team's involvement, and consequently had lower rates of rejection across all risk factor domains: medical factors, treatment adherence, family factors, social support, psychiatric history, substance misuse, financial stability, and relationship to their medical

team. Figure one shows a socioecological model highlighting social determinants of health and related factors assessed by the team as being relevant to patient adherence.

The same chart review study suggested that the incidence of rejection was higher for those with lower levels of social support. It also demonstrated that 57% of patients followed by the nephrology team met risk for non-adherence, independent of psychological functioning markers. This data was collected via the Parent Medication Barriers Scale (PMBS) and the Adolescent Medication Barriers Scale (AMBS). The team's results suggested a high risk for developing rejection within one year of completing these scales. The team also studied specific psychosocial outcomes in the form of psychiatric diagnoses. Of those patients without a psychiatric diagnosis prior to transplant (72.5%), 32% experienced new onset of a psychiatric diagnosis post-transplant. These diagnoses included adjustment disorder, anxiety, depression, and/or suicidal ideations. Overall, 43% experienced psychosocial complications post-transplant (Nguyen & Logan, 2019).

Given this research base and the highlighted gaps across the literature and national practice in combination with CHP's chart review retrospective study, the CHP kidney transplant psychosocial team (transplant psychologist and transplant social worker) formulated a post-transplant assessment pilot program and non-adherence protocol to assess if modifiable barriers can be appropriately identified and addressed. Through the retrospective chart review previously described, they discovered that only 18% of patients received psychosocial intervention before rejection, and those deemed high risk across biopsychosocial markers prior to transplant were less likely to have rejection episodes post-transplant (Nguyen & Logan, 2019).

The team developed the novel protocol highlighted in this paper in order to ensure access to the psychosocial team while identifying and addressing barriers to adherence in a standardized manner with collaboration across the medical team. Overall, they aimed to identify barriers to

adherence and effectively address these applicable barriers through the systematic protocols discussed in this paper, while improving overall health outcomes for pediatric kidney transplant patients. Through an integrated clinic setting, patients and families can be systematically evaluated for barriers to adherence, concerns, and subsequent connections to larger social determinants of health through psychosocial services. This specific study assesses the pilot program processes while analyzing rates of completion, reach, feasibility in terms of a UPMC Quality Improvement Project, and overall non-adherence themes.



**Figure 1: Socioecological Model of Pediatric Transplant Adherence**

## **3.0 Methods**

### **3.1 Study Sample**

Eligible participants were post-transplant patients followed by the CHP main campus kidney transplant team, unless excluded due to current graft loss, death, and/or status of being re-listed for a second transplant. Based on this criterion, 148 patients and families were eligible for post-transplant annual evaluations in the first year of data collection. Surveys were administered to patients and families in various forms at the 30-day, 3-month, and 6-month post-transplant marks in addition to the annual evaluations which serve as the subject of this paper. Surveys were included based on their ability to assess realistic predictors of biopsychosocial risk and associated barriers to adherence, and these are further discussed in the Measures Section.

### **3.2 Study Design**

Through this study and novel program, the CHP kidney transplant team aimed to identify barriers to adherence among eligible participants, address these barriers, and improve overall health outcomes of those included. Effective attention to these identified barriers included additional involvement of the integrated medical team, referrals to resources, and/or the application of systematic non-adherent protocols highlighted in this paper. Although the latter is not an explicit part of this particular quality assurance initiative, it is important to include the



protocols created in response to these annual evaluations. This component represents a secondary aim, and was incorporated in the integrated team's processes and response.

Universal screening via standardized surveys began in Fall 2018. For the purpose of this paper, year one data collection and completion rates are presented in addition to pilot program alterations made prior to transitioning into year two data collection and the subsequent effects on completion rates. Pediatric renal transplant patients and their parents/guardians followed by the nephrology team at the Children's Hospital of Pittsburgh (CHP) completed a collection of items and measures as a component of collaborative standardized clinical care delivered in an integrated outpatient clinic and/or inpatient setting. Evaluations were originally dispersed through paper forms during clinic visits in an integrated setting. After months of utilizing this form of data collection, the project was approved as an official UPMC Quality Improvement Project and was transitioned into the online RedCap data management system. Prior to this, surveys were scored and data was coded in the patient's electronic medical chart in the appropriate section. After the transition to the Quality Improvement Initiative, surveys were administered on UPMC approved electronic tablets through RedCap, creating immediately accessible data. Assessments completed prior to this date were manually entered into RedCap by the Transplant Psychology Fellows in order to provide completeness for data analysis.

The psychosocial team aimed for three main levels of reach (i.e., survey completion and assessment) based on the designed established protocol for year one data collection. The first protocol aim intended to reach patients in clinic within their transplanted annual quarter. Next, the team aimed to reach patients in clinic within the year one data window. Newer transplants were reached as close to the one-year mark of their transplant date as possible. Lastly, the team completed outreach via phone to complete missed in-person annual evaluations. Systematic

outreach protocol included two phone calls per family at separate dates using the phone numbers listed in the medical chart. If reached in this manner, the project was thoroughly explained to the patient and/or caregiver. Secure emails were then sent to the provided and preferred contact email, including a personalized direct survey link from the RedCap system with instructions. Progress was tracked in the RedCap system in order to assess completion, and identifiers were applied to each survey in the form of name and date of completion in order to ensure proper tracking.

The processes utilized in each post-transplant clinic were systematic and interdisciplinary. Prior to each clinic, members of the integrated team attended “Pre-Visit Planning Meetings,” where patients for the following clinic date were thoroughly discussed regarding all care aspects and potential concerns. Present at these meeting included the following: nephrologist, transplant coordinators (three total), transplant social worker, transplant psychologist, and the transplant data coordinator. During this time, patients were scheduled for their annual assessment to be completed in the integrated clinic setting. In clinic, the flow remained consistent with the transplant coordinator completing medical assessments first followed by the attending physician. The psychosocial team coordinated annual assessments and meetings with patients in the designated psychosocial clinic room or the patients’ respective clinic rooms. The clinic used white boards to track patients eligible for annual assessments and completed annual assessments. This particular setup was utilized to ensure proper clinic flow, while increasing access to all pertinent team members in a systemized manner.

Surveys were explained and consent was obtained verbally from a member of the psychosocial team upon display of the letter accompanying each survey. Families were provided with the applicable surveys via paper or electronic tablets designed to take less than 20 minutes. Prior to the patient and family leaving clinic, clinical cutoffs were calculated for each survey by a

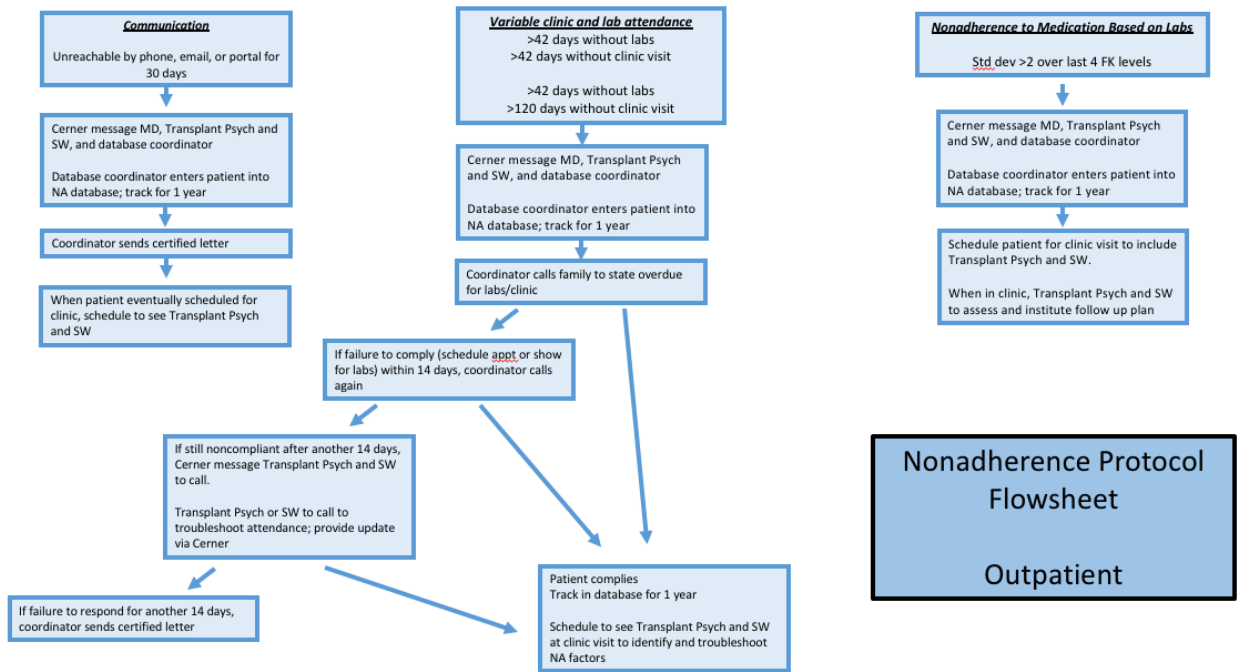
transplant psychology fellow. If their scores were at or above the clinical cutoff, they met with the psychosocial team in-person to further review and address concerns. However, the psychosocial team aimed to follow-up with each family upon completion of the annual evaluations regardless of scores. Additionally, if patients were admitted for rejection with non-adherence lab markers or suspected medication non-adherence, surveys were administered to patients while inpatient. Non-adherence protocol was applied when necessary based on the highlighted factors.

### **3.2.1 Non-Adherence Protocol**

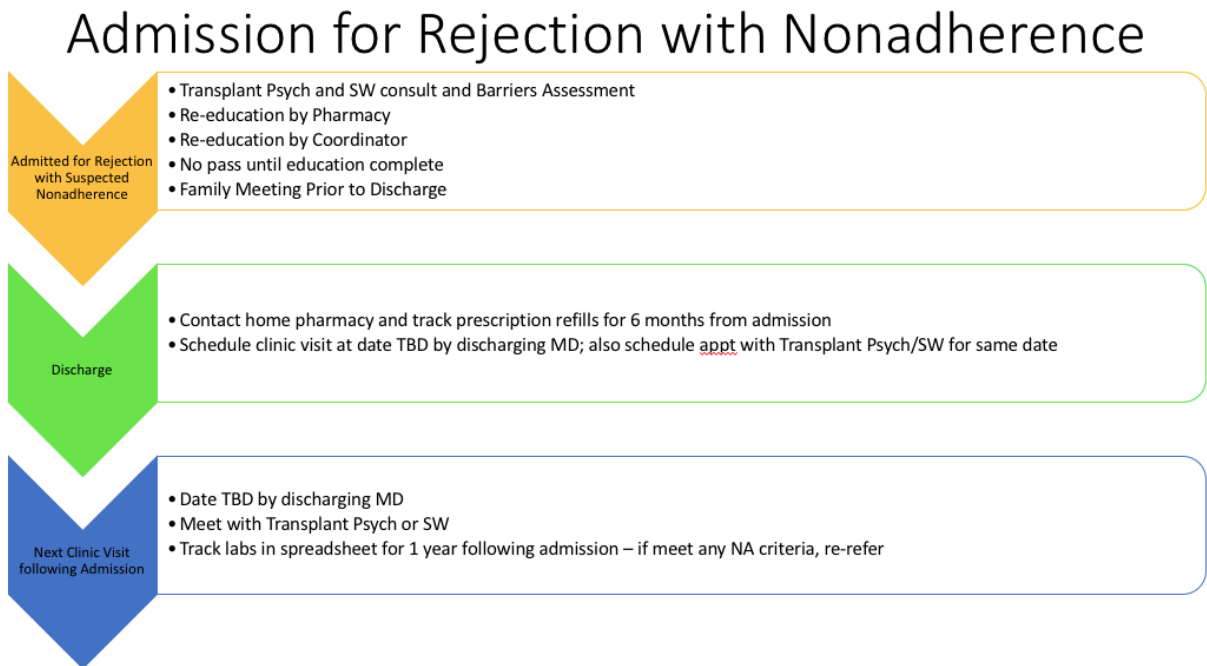
Although not a part of the quality assurance initiative, it is important to include the protocols created in response to these annual evaluations. This represents a secondary study aim, and continues to be incorporated in the integrated team's processes and response. Patients can "flag" for non-adherence based on multiple markers including lab levels, lack of contact greater than 30 days, missed clinic and/or lab draws greater than 42 days, and screening results from the PMBS or AMBS. This systematic monitoring is assessed by the interdisciplinary team including nephrologists, transplant coordinators, transplant psychologist, and the transplant social worker. If the patient flags for non-adherence markers on an outpatient basis, the team follows the Non-adherence Protocol Flowsheet Outpatient as shown in Figure Two at the conclusion of this section. Patients are then entered into a secure database and followed for one-year following the date they flagged for non-adherence. If a patient flags for suspected non-adherence upon admission to the hospital for a rejection episode, the team initiates a different protocol flowsheet as shown in Figure Three at the conclusion of this section. Similar protocol is utilized, but the team administers the Barriers Assessment while the family is inpatient status. Education meetings are arranged with the

patient, family, pharmacy, transplant coordinator, and psychosocial team members during the inpatient stay.

Overall, these systems and processes are not intended to elicit fear or guilt in the patient and family unit, and are not described as a punishment protocol. Instead, these processes secure access to and the involvement of all pertinent medical team members to ensure the patient and family are fully supported while addressing potential barriers that inevitably exist in many cases. Concomitantly, the team can systematically address these scenarios and apply various resources when necessary. Families are followed for the one-year time window with consistent monitoring of a combination of the following components: lab levels, maintaining contact with the medical team, attending outpatient clinic appointments, and/or tracking medication refills from the associated pharmacy. Patients and families can re-qualify for this one-year time period based on repeated markers which would then restart the time window.



**Figure 2: Outpatient Nonadherence Protocol Flowsheet**



**Figure 3: Inpatient Nonadherence Protocol**

### 3.3 Measures

#### 3.3.1 Psychosocial Measures

The medical team included the selected measures as they represent validated timely surveys that would likely reflect realistic predictors of psychosocial risk and barriers to adherence. Surveys included in the annual assessments consisted of the following: Initial Survey, Annual Demographic Form, Adolescent Demographic Form, Annual Demographic Form 18+, Family Functioning Questionnaire (FAD), Pediatric Symptom Checklist (PSC), Multidimensional Scale of Perceived Social Support (MSPSS): Parent, Multidimensional Scale of Perceived Social Support (MSPSS): Adolescent, Patient Health Questionnaire-9 (PHQ-9), Medication Assessment Parent Version (PMBS), Pediatric Symptom Checklist (PSC), Youth Pediatric Symptom Checklist (Y-PSC), Posttraumatic Stress Disorder Checklist (PCL-5), Medication Assessment Self Report (AMBS), and PedsQL Family Impact Model. All represent validated surveys except the Impact Questionnaire, as this specific measure was created by the transplant psychosocial team to address areas of concern based on clinical experience. The psychosocial team collaborated with the transplant coordinators to create the Impact Questionnaire in order to address the following domains: risk, demographics, impact, burden, self-efficacy, and overall quality of life markers. The self-efficacy questions reflect notions of health literacy, although the team chose to not utilize this terminology in the assessment.

The collective combination of surveys depended on the survey arm administered as previously mentioned, and these are outlined in Figure Four below. The chosen measures via a collection of established surveys vary based on the patient's age at the time of evaluation completion. Parental completion of measures were collected for patients 17 years and younger.

For patients age 11 and older, self-report measures were collected if developmentally appropriate. Survey collections correlated directly with age, and the following data sets were utilized: Arm 1 (birth through four years), Arm 2 (age five through ten), Arm 3 (parent form of age 11-17), Arm 4 (patient form of age 11-17), and Arm 5 (ages 18 and older). If the patient was diagnosed with a developmental delay, the parent/guardian was asked to complete Arm 2 or Arm 3 based on the Transplant Psychologist’s diagnostic assessment and degree of developmental delay.

Post-Transplant Annual Packet Components Age Bracket:	Arm 1 0-4	Arm 2 5-10	Arm 3 11-17 Parent	Arm 4 11-17 Teen	Arm 5 18+
<i>Letters to Accompany Annual</i>					
Letter for Ages 0-4	x				
Letter for Ages 5-10		x			
Letter for Ages 11-17			x		
Letter for Adult 18+					x
<i>Survey</i>					
Demographic Form/Transplant Care Questionnaire	x	x	x		x
CBCL 1.5-5	x				
Short FAD	x	x	x		x
MSPSS	x	x	x	x	x
PMBS	x	x	x		
AMBS				x	x
PSC		x	x		
Y-PSC				x	
PCL-5				x	x
PHQ-9					x

**Figure 4: Annual Evaluation Components by Age**

### 3.3.2 Medical Measures

Objective medical measures were also incorporated in the protocol to identify and address potential non-adherence and subsequent barriers to the lack of adherence further highlighting the necessity of a collaborative interdisciplinary team. Patients and families can flag for non-adherence

based on the following criteria in combination with the aforementioned psychosocial evaluations: lab values, missed clinic and/or lab draws greater than 42 days, and not reachable via established contact protocol for greater than 30 days. Lab value monitoring consists of FK levels using the Medication Level Variability Index (MLVI), with a standard deviation of two across the most recent four results. The team is in the process of receiving IRB approval, which would allow for the direct connection between these two databases and subsequent dissemination of data linking evaluation results with medical markers.

### **3.4 Pilot Program Changes**

It is important to note changes made from year one to year two of data collection as this represents a working pilot program, and process alterations likely affect rates of completion. Based on concerns that surfaced during year one data collection, some items were altered by the psychosocial team prior to progressing into year two. As socio-economic status (SES) is thoroughly assessed in pre-transplant evaluations, this item was incorporated into the demographic form via income brackets to better assess financial changes or concerns of the family unit. Furthermore, change in housing address was added to assess potential housing instability. A question pertaining to different services, benefits, and agencies involved was further specified to include the following options: SSI/SSDI Benefits, WIC, SNAP (e.g., food stamps), School Lunch Vouchers, Medicaid, Medicare, MATP (e.g., subsidized transportation for medical appointments), and State Waivers. As the integrated team plays a crucial role in arranging many of these resources, they aimed to assess stability across resources and address any present concerns relating to these factors. To better streamline risk components and the connection to non-adherence, the team added



a Risk Assessment Questionnaire comprised of the following attributes: CRAFFT (validated substance use screening tool), a question assessing feeling safe at home, and concerns the patient may wish to discuss privately with a member of the psychosocial team. Due to the complexity of parental consent, the Risk Assessment Questionnaire was only added to Arm 5 to assess those age 18 and older.

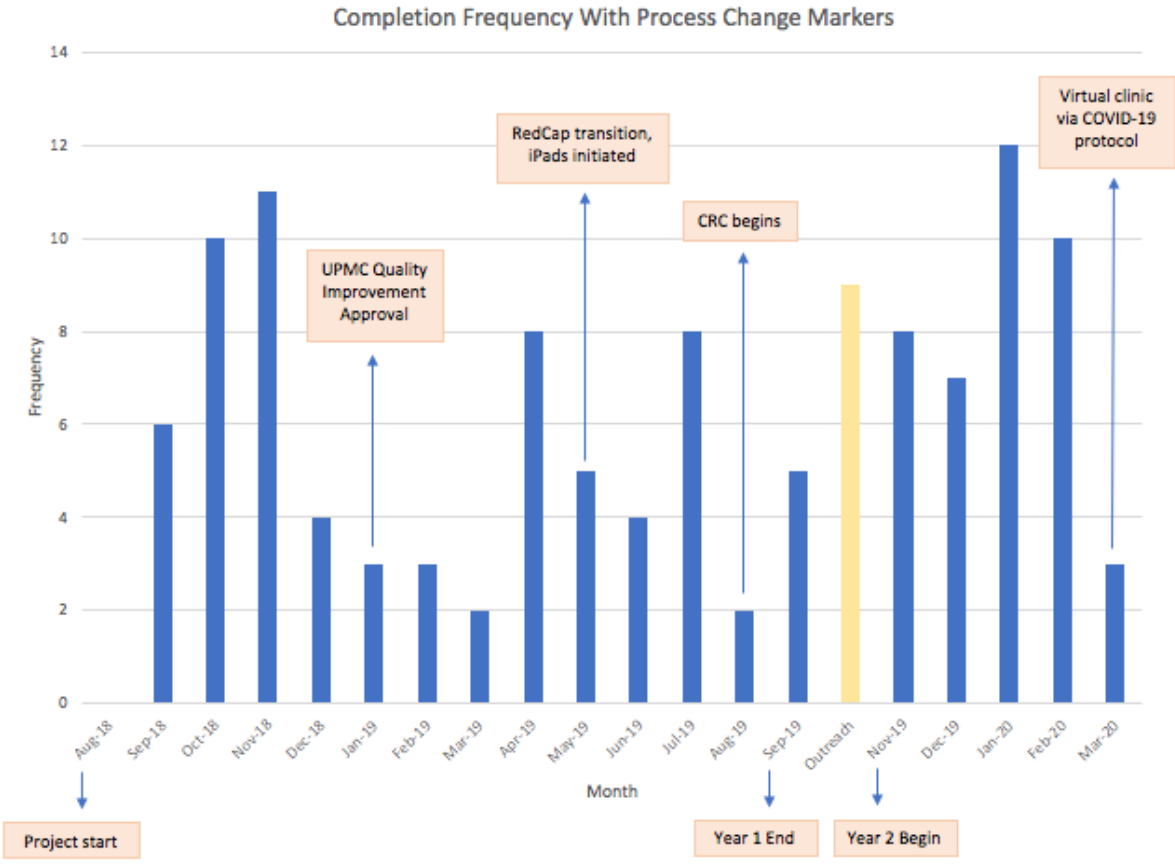
Process changes were incorporated throughout the project. Upon approval of a UPMC Quality Improvement status, two electronic tablets were obtained to provide for completion in clinic. This reduced the need for paper forms, in addition to the need to manually enter data into the RedCap system and scoring in the respective patient's chart. A Clinical Research Coordinator (CRC) position was added in September 2019 to complete the outreach portion of year one data collection. Upon this completion, the CRC integrated in the clinic setting to improve administration of the annual evaluations and to polish clinic flow. The suggested effects of these process changes on completion rates can be viewed in Figure Five at the conclusion of this section. Important process changes and key project dates are listed below.

- Project start: August 2018
- Year 1 data collection being: September 2019
- UPMC Quality Improvement Project Approval: January 2019
- Year one data collection end: September 2019
- Conversion to RedCap completed and electronic tablets initiated: May 2019
- Outreach protocol: September 2019 – October 2019
- Year two data collection begin: November 2019
- Clinical Research Coordinator (CRC) starts: August 2019

- Virtual clinic via COVID19 protocol: 3/18/20, psychosocial assessments implemented via outreach protocol

### **3.5 Analysis**

Inclusion criteria for annual evaluations consisted of all post-transplant patients followed by the CHP Nephrology Team as previously highlighted. Exclusion criteria was applied when assessing those eligible for participation in the pilot program data measures and subsequent analyses of completion. Those excluded include the following statuses: graft loss, listed for a second transplant, and/or patient was deceased. Rates of completion and overall reach were assessed using the RedCap system in combination with a secure UPMC database consisting of medical record information and dates of completion. Descriptive statistics and frequencies through RedCap and SPSS were used to analyze the available deidentified data regarding major themes of non-adherence suggested through this program.



**Figure 5: Process Changes and Effects on Evaluation Completion Frequencies**

## 4.0 Results

### 4.1 Reach and Completion

As a quality assurance program, assessing reach and completion rates were deemed priority at the start of the pilot program in order to demonstrate feasibility and potential effects in a healthcare delivery system. Of the 148 eligible for annual post-transplant evaluations, the team completed annual evaluations on 82 patients and parents/guardians if applicable based on age demographics as highlighted in the methods section of this paper. Below are the three aims of completion previously outlined, and numbers of patients and families reached through each corresponding aim.

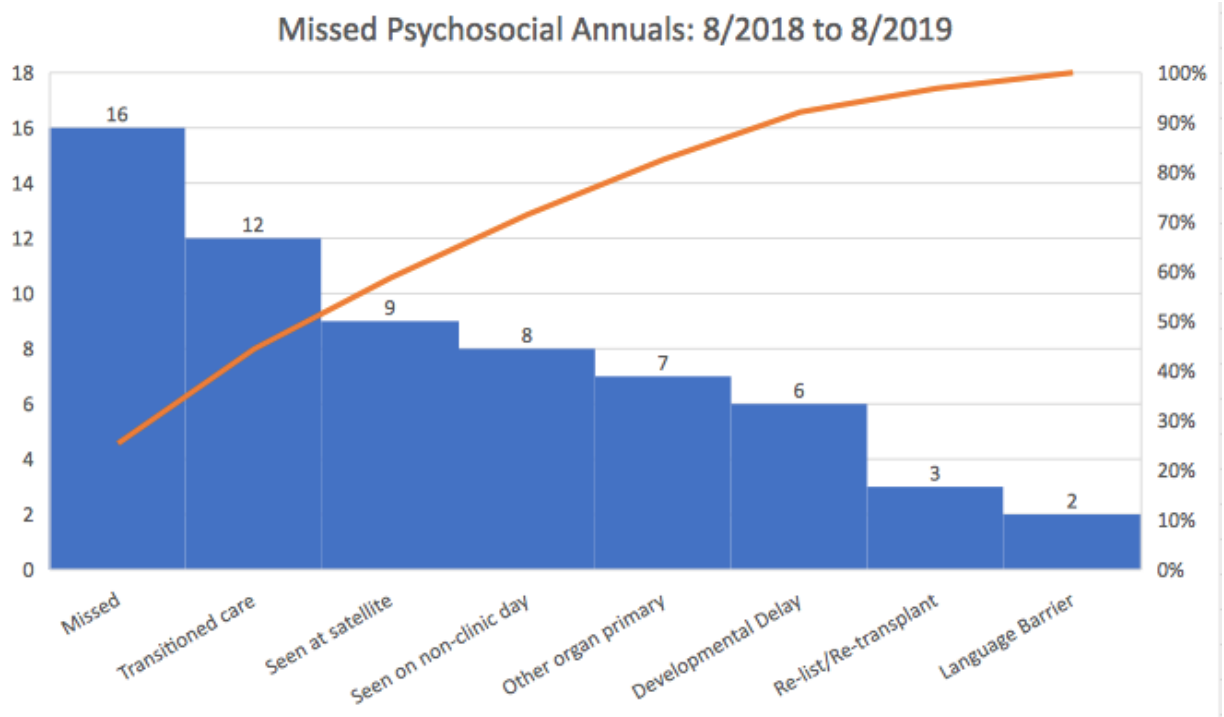
- AIM 1 (Reach patients in clinic within their transplanted year quarter within year one data collection window): 37 patients reached and evaluations completed.
- AIM 2 (Reach patients in clinic within the year one data collection window): 36 patients reach and evaluations completed.
- AIM 3 (Systematic outreach protocol completed in September and October 2019 in attempts to reach those not completed in initial protocol): 9 patients reached and evaluations completed. When obtaining consent, one family expressed preference for completing in-person in clinic versus virtually through email, and they were reached in their next clinic visit during year two data collection.

Year one data completion was tracked in RedCap and the UPMC One Drive system. Upon completion of year one, completion themes and results were thoroughly assessed. Prior to

assessing reasons for non-completion, two important themes surfaced including partial completion and application of the incorrect data arm. During the transition to electronic tablets, one patient was provided with the wrong collection of assessments (i.e., provided with Arm One instead of Arm Five). Partial completion per data arm are as follows: one partial (Arm Two), two partial (Arm Three), two partial (Arm Four), and one partial (Arm Five). The 66 eligible annual evaluations not completed were thoroughly assessed by the psychosocial team and reasons for non-completion were individually applied and coded. Reason codes included are described below. Figure Six displays a Pareto chart with reasons and lack of completion numbers applied to each corresponding reason:

- Missed: no coded explanation. Patient could have been missed due to ineffective clinic flow, checked out prior to being seen by psychosocial team, were deemed not clinically appropriate at time of clinic appointment, were admitted for further hospital evaluation, and/or were deemed as lost to follow-up (i.e., lack of communication with medical team over a one-year time period).
- Transitioned Care: Patient and family could have moved to other state consequently transitioning care to outside institution, or patient transitioned to adult care.
- Seen at Satellite: Patient seen at CHP satellite clinic, and therefore lack access to integrated healthcare team. Some patients seen at a CHP satellite were included in completion rates based on outreach protocol.
- Seen on non-clinic day: Patient scheduled for other day deemed not a Nephrology Transplant Clinic day. Therefore, patient did not have access to interdisciplinary clinic team.

- Other Organ Primary: Patient has multiple solid organ transplants including kidney, and is followed primarily by other organ transplant team (e.g., heart, lung, abdominal, and/or liver).
- Developmental Delay: Patient deemed developmentally inappropriate to complete per Transplant Psychologist’s assessments and historical diagnoses via the medical chart.
- Re-List/Re-Transplant: Patient has been re-listed for a second kidney transplant due to graft loss, or has recently been re-transplanted.
- Language Barrier: Patient and family rely on CyraCom interpretation services which do not currently have the capacity to complete the annual assessments virtually.



**Figure 6: Pareto Chart of Non-completion Rates and Reasons**

## **4.2 Data Themes: What Have We Learned**

### **4.2.1 Annual Assessment Themes**

Many of the data themes that surfaced through these assessments relate to psychosocial care components, social determinants of health, and various barriers to adherence, whether these connections are direct or indirect. Some of these major themes from year one data are discussed here, and more advanced statistical measures will be completed upon IRB approval connecting the RedCap database to objective medical measures as previously discussed. Nearly 17% of patients and families reported missing a clinic visit in the previous year and note the corresponding reason for missing as follows: not having a reliable vehicle (22.2%), financial hardship (11.1%), inability to take time off of work (11%), and others such as scheduling conflicts and/or forgetting to schedule an appointment. Nearly 80% of those surveyed reported worrying about outcomes of monthly lab work at least a little bit, with about 30% worrying often. When addressing educational aspects, 40.4% reported significant absences from school, and 36.1% reported a negative impact on grades. The Y-PSC results suggest that 20.6% admit to taking unnecessary risks. The specifics of these results are distinct to each patient, and addressed one-on-one depending on the situational nature. When assessing the MSPSS data, 72.9% reported high overall perceived support, with 27.1% reporting low to moderate overall support.

Just over 45% of patients were flagged for non-adherence risk based on the clinical cutoff scores calculated from PMBS, or had clinically significant barriers to adherence. The AMBS results suggest that around 30% reported experiencing forgetfulness and admitted to not taking medications matching the prescribed dose and frequency, yet only 4.3% admitted to disorganization with when and how to take necessary medications which could suggest other

factors affecting the forgetfulness. Over 26% of adolescent and adult respondents self-reported being tired of taking medications, and over 31% reported being tired of living with a medical condition.

Based on this data, overall predictive value themes surfaced. The PMBS total scores were clinically predicted by the MSPSS, yet not predicted by the FAD. The PMBS and MSPSS were negatively correlated ( $r = -.40, p < .01$ ). Concurrently, the FAD did not significantly relate to the MSPSS. The theme of parental stress did not seem to correlate significantly with the PMBS scores. When adjusting for differences between adherence groups (i.e., two or more barriers reported vs. zero to one barriers), they did not differ significantly on the following: FAD, MSPSS, or confidence report. However, the adherence groups did differ on reported parental stress ( $t(49) = 2.40, p < .05$ ), or caretakers of patients with clinically significant barriers to adherence reported greater levels of stress ( $M \text{ stress} = .91$ ) compared to caretakers of patients without clinically significant barriers ( $M \text{ stress} = .55$ ).

#### **4.2.2 Clinical Themes**

Additionally, through the standardized surveys administered, many other needs and concerns surfaced through these processes, evaluations, and the supportive nature of the integrated clinic. Concerns for comorbidity of mental health conditions surfaced, such as depression, anxiety, suicidal ideations, and attention deficit hyperactivity disorder (ADHD). Some examples of other concerns are as follows: unsafe housing, significant mold in housing, suicidal ideations, lack of transportation, education concerns, domestic violence, drug use, risky behaviors among adolescents, financial concerns, community violence, electricity getting shut off, inability to pay necessary bills, and overall lack of means/tools (e.g., no cell phone). This suggests the continual



need for the direct involvement of psychosocial team members in the clinic setting in order to address potential barriers, diagnoses, and emergent needs often reflecting social determinants of health as they arise throughout the treatment continuum. Many of these concerns arguably would not have surfaced if standardized assessments were not applied and subsequently linked to the psychosocial team members.

### **4.2.3 Clinical Response**

Consequential interventions depending on each individual's assessment were specifically tailored to that patient and their family. From the arguable needs assessment based psychosocial evaluations, results initiated tailored responses including education, transition resources, insurance, transportation, and overall financial resources. Examples of applied interventions include the following: orientation to medication phone applications, assistance with sorting medications, application of pill boxes, organizing transportation services, financial assistance, admission to hospital if necessary, referral to psychological services, correspondences with schools if IEP (legally binding document for students with required special education services) or 504 plans (do not meet special education criteria but still require medical accommodations) are in place and/or needed, general health education, and comprehensive referrals to resources. The above results highlight the importance of targeting each intervention addressing barriers to adherence to the individual based on their respective results via clinical cut-off scores and overall results from the annual evaluations and clinical interactions.

Throughout year one, seven patients flagged and were entered into the tracking database, and the team subsequently initiated the respective non-adherence protocol per flowsheets previously highlighted. The four main areas resulting in flagging are as follows: lack of

communication (>30 days), no labs or clinic (>42 days), labs (2 standard deviations over last four FK levels), and annual screenings. As this represents a novel pilot program, the tracking database and non-adherence protocols were not consistently utilized as the quality assurance aims focused on the post-transplant evaluations. As previously discussed, the team is in the process of receiving IRB approval, which would allow for the direct connection between the two databases and subsequent dissemination of data linking evaluation results, medical markers, and application of non-adherence protocols.

## **5.0 Discussion**

### **5.1 Limitations**

As with any research, limitations exist in this pilot program study. The nature of evaluative surveys utilized as the method for data collection have inherent biases related to self-reporting. Reporting bias represents one limitation, as patients and family members may purposefully suppress information. With this, those lost to follow-up or those that did not complete the annual surveys may differ from those represented in the data highlighting a form of selection bias. The individuals not represented may add significant results to the team's data. The team attempted to limit this aspect of bias through the outreach protocol at the conclusion of year one, yet the overall reach only increased slightly from these time-consuming processes suggesting overall ineffectiveness. Additionally, recall bias represents another limitation due to the retrospective measures collected by the selected surveys. The team believes interviewer bias may still be present, yet was decreased when the transition from paper forms to electronic tablets occurred. Privacy was granted to patients and families before the initiation of survey completion unless the presence of a team member was directly requested by the family. The latter situation only occurred once, as the guardian wanted to ensure language barriers were properly addressed during the completion.

Internal validity is assessed as being moderate, as the team used established valid measures in the annual evaluations, with the exception of the demographic forms highlighted in the methods section of this paper which were informed by the team's clinical practice. Although a definitive cause and effect relationship cannot be stated at this time, the results suggest correlations between multiple measures and barriers to adherence. The team can increase internal validity when the

connection of the two databases is permitted (i.e., RedCap assessment data and objective medical measure data). Furthermore, as this study represents a working pilot program, the internal validity likely fluctuates as changes are made. Likely threats to internal validity include biases previously mentioned and potential confounding factors. The results uncovered at CHP may not be generalizable to all pediatric transplant patients as circumstances may vary by transplant center. However, inclusion and exclusion criteria were applied in order to strengthen external validity. As the pilot program continues to move forward as an approved Quality Improvement Project, the team can utilize replication to further enhance external validity prospectively.

## **5.2 Discussion and Recommendations**

The CHP kidney transplant team conducted this study to identify barriers to adherence while addressing these barriers in an integrated delivery system through a novel approach. The results of this pilot program show the potential impact of identifying and effectively addressing the existence of non-adherence and barriers to adherence through an interdisciplinary, systematic approach in an integrated delivery system. Although a working pilot program, CHP has demonstrated that programs are feasible and can have potential long-term effects. By demonstrating the feasibility of these processes, they can be implemented in various settings and populations that experience the costly effects on expenditures and health outcomes associated with medical non-adherence. However, it is important to note that teams should tailor the protocol to meet the needs and parameters of the specific intended target population.

As this pilot program has progressed since the initiation, the psychosocial team has received increasing levels of support and buy-in from CHP medical team members. Pertinent

interdisciplinary team members have become increasingly cognizant that patients are not missed in clinic, and work diligently to ensure evaluations are complete. The entire team has quickly realized the implications of adding a clinical research coordinator position, and the positive effects on clinic flow, completion rates, and access to the psychosocial team. These process changes highlighted in this paper will continue to be assessed as the project continues and evolves.

The highlighted limitations inspire various areas of improvement for future work with this pilot program and outside entities seeking similar programs. In order to increase completion rates, the assessments could be translated to address language barriers as CHP performs transplants on international patients from various countries. Although data collection remains ongoing, concerns that surface during clinic point to potential alterations in the future and expansion of methods used. As the results suggest a link between social determinants and barriers to adherence, the team should continue to screen for these items such as those added for year two (e.g., safe housing, income/SES, and changes in agency involvement). Assessments to address risky behaviors and domestic violence were added to Arm Five of data collection (age 18+), but this could be expanded to the adolescent demographics if legally approved. Parental consent represents a concern as the adolescent survey arm covers ages 11-17, leading the team to currently exclude this addition for this age demographic. Additional social determinants could include but are not limited to food insecurity and more direct questions related to stable housing. Future work could include a flagging protocol mechanism to alert the team that an emergent need exists (e.g., electricity shut-off, issues with essential utilities, food insecurity, eviction, suicidal ideations, etc.) as current UPMC database systems possess this capacity for certain screeners such as the CRAFFT assessment. With this, a patient flags in the Cerner charting system based on their CRAFFT survey completion, automating a task response from a medical team member.

From a public health perspective, the team could expand health literacy measures as this represents a key component of the collaborative team relationship as highlighted in the adherence definitions. A demonstrated disconnect exists between patient/family abilities and healthcare communication in many clinical settings. Furthermore, low health literacy levels directly correlate with the costly effects highlighted in this paper, such as increased healthcare expenditures, increased risk of hospitalizations, and poorer health outcomes. These factors further support the inclusion of greater assessment of health literacy in clinical settings, and could be incorporated into this pilot program.

Long-term implications of early identification of barriers while working to effectively address these aspects of care need to be further assessed prospectively as the pilot program continues. The impact of initiating the non-adherence protocol and tracking patients for one year after their entry into the non-adherent database will need to be thoroughly assessed for impact on outcomes and overall effectiveness. More specifically, the team will assess overall effects on cases of rejection and admissions related to the non-adherence protocol and subsequent data from these annual assessments. These specific results could further support the suggested effectiveness of targeted preemptive and preventive interventions.

Every transplant journey is different and complex in nature, with each being directly and indirectly affected by health factors, social determinants, and circumstance. Thus, approaches must be systematic in nature, yet tailored in response to each individual, family, and the circumstances surrounding their care. The work completed in this pilot program begins this process and demonstrates the feasibility of implementing similar protocols in integrated healthcare delivery systems. Although non-adherence represents a common and often detrimental factor in transplant rejection and outcomes, research and subsequent protocol to address these elements are far less

common both in theory and practice across the national system. If the system is to label patients as “non-adherent” and/or “non-compliant,” then medical teams have an arguable ethical obligation to properly identify barriers that exist and work to systematically address the respective concerns related to each patient and family. Furthermore, hospital systems should recognize the financial and status incentives to implementing programs such as this, and support their medical teams accordingly to help foster truly integrated, holistic approaches to pediatric transplant care.

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