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Medication, Healthcare Follow-up, and Lifestyle Nonadherence: Do They Share the Same Risk Factors?

Yue-Harn Ng, MD,[1,2] Igor Litvinovich, MS,[1] Yuridia Leyva, MS,[3] C. Graham Ford, MS,[3] Yiliang Zhu, PhD,[4] Kellee Kendall, MPH,[5] Emilee Croswell, BA,[6] Chethan M. Puttarajappa, MD,[6] Mary Amanda Dew, PhD,[7] Ron Shapiro, MD,[8] Mark L. Unruh, MD,[1] and Larissa Myaskovsky, PhD[1,3]

Background. Barriers to medication adherence may differ from barriers in other domains of adherence. In this study, we assessed the association between pre–kidney transplantation (KT) factors with nonadherent behaviors in 3 different domains post-KT. **Methods.** We conducted a prospective cohort study with patient interviews at initial KT evaluation (baseline—nonadherence predictors in sociodemographic, condition-related, health system, and patient-related psychosocial factors) and at ≈6 mo post-KT (adherence outcomes: medications, healthcare follow-up, and lifestyle behavior). All patients who underwent KT at our institution and had ≈6-mo follow-up interview were included in the study. We assessed nonadherence in 3 different domains using continuous composite measures derived from the Health Habit Survey. We built multiple linear and logistic regression models, adjusting for baseline characteristics, to predict adherence outcomes. **Results.** We included 173 participants. Black race (mean difference in adherence score: –0.72; 95% confidence interval [CI], –1.12 to –0.32) and higher income (mean difference: –0.34; 95% CI, –0.67 to –0.02) predicted lower medication adherence. Experience of racial discrimination predicted lower adherence (odds ratio, 0.31; 95% CI, 0.12–0.76) and having internal locus of control predicted better adherence (odds ratio, 1.46; 95% CI, 1.06–2.03) to healthcare follow-up. In the lifestyle domain, higher education (mean difference: 0.75; 95% CI, 0.21–1.29) and lower body mass index (mean difference: –0.08; 95% CI, –0.13 to –0.03) predicted better adherence to dietary recommendations, but no risk factors predicted exercise adherence. **Conclusions.** Different nonadherence behaviors may stem from different motivation and risk factors (eg, clinic nonattendance due to experiencing racial discrimination). Thus adherence intervention should be individualized to target at-risk population (eg, bias reduction training for medical staff to improve patient adherence to clinic visit).

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Kidney transplantation (KT) provides improved survival for patients with end-stage kidney disease compared with remaining on dialysis.[1] However, to maintain the viability of a kidney allograft post-KT, patients are required to adhere to (1) complex medical regimens,[2,3] (2) healthcare follow-up (laboratory testing and clinic attendance),[4,5] and (3) engagement in healthy lifestyle behavior (eg, following diet and exercise plans, abstinence from substance use, and blood pressure monitoring).[6-8] According to the World Health Organization (WHO), adherence is defined by the extent to which a person's

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[1] Division of Nephrology, Department of Internal Medicine, University of New Mexico, Albuquerque, NM.

[2] Division of Nephrology, Department of Medicine, University of Washington, Seattle, WA.

[3] Center for the Healthcare Equity in Kidney Disease (CHEK-D), University of New Mexico Health Science Center, Albuquerque, NM.

[4] Division of Epidemiology, Biostatistics and Preventive Medicine, Department of Internal Medicine, University of New Mexico, Albuquerque, NM.

[5] Highmark Health, Pittsburgh, PA.

[6] Department of Medicine, School of Medicine, University of Pittsburgh, PA.

[7] Department of Psychiatry, School of Medicine, University of Pittsburgh, PA.

[8] Mount Sinai Recanati/Miller Transplantation Institute, Icahn School of Medicine.

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Correspondence: Larissa Myaskovsky, PhD, MSC 04-2785, 1 University of New Mexico, Albuquerque NM 87131. (lmyaskovsky@salud.unm.edu).

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behavior—taking medication, following a diet, etc, corresponds with agreed recommendations from a healthcare provider.[9] Immunosuppressant medication nonadherence is one of the leading causes of post-transplant de novo antibody production, acute rejection, and allograft loss.[10-13] Literature reviews report a crude prevalence rate of medication nonadherence ranging from 8% to 67% within 1-y posttransplant,[10,11,14-16] with increasing prevalence with time after transplant.[17] The wide variation in the prevalence of medication nonadherent behavior may be related to differences in the measurement tools used (eg, self-report versus drug levels versus pharmacy refill history[18]) as well as the different definitions of nonadherence used at different centers.[19,20]

In addition to medication nonadherence, KT recipients have been reported to have relatively high rates of nonadherence in other domains as well, with 5%–15% not adhering to healthcare follow-up annually and 22%–31% not adhering to lifestyle recommendations annually.[8,18,21] All these behaviors can contribute to poor patient outcomes, including allograft loss, posttransplant weight gain, and diabetes.[4,5] Current literature and interventions have focused overwhelmingly on medication adherence with few looking at adherence to healthcare follow-up[4,5] or lifestyle.[7,8] From a patient perspective, studies have demonstrated that patients tend to be more adherent to medications than to lifestyle recommendations.[6,7]

Adherence behavior can be influenced by different factors, including healthcare system, sociodemographic, condition-related, treatment-related, or patient-related factors.[9] Risk factors associated with posttransplant nonadherence include younger age, lack of social support, minority race, geographical distance from transplant center, unemployment, cognitive impairment, illness perception, poor mental health, and beliefs about, or satisfaction with, medications.[15,22-29] To date, no prospective study has assessed the risk factors of all 3 domains of adherence (ie, medication, healthcare follow-up, and lifestyle behavior) in kidney transplant patients concurrently. We believe that nonadherence in any or all 3 domains can potentially contribute to poor allograft outcomes.

Early recognition and ability to identify patients who are at risk for post-KT nonadherence in any domain would allow transplant teams to intervene pre- and post-KT, and possibly improve patient outcomes (eg, multidisciplinary intervention of medication nonadherence pre-KT or referral to exercise programs to increase activity levels before KT). For this study, we assessed risk factors as defined by the WHO risk factors for nonadherence in chronic disease[9] to predict nonadherence behaviors post-KT. We aimed to identify pre-KT factors at the time of initial KT evaluation that are associated with nonadherence behaviors posttransplant in 3 distinct domains, with the hope that it will allow for earlier interventions both pre- and post-KT in future studies.

MATERIAL AND METHODS

Study Design and Procedures

We conducted a prospective cohort study of KT patients at the University of Pittsburgh Medical Center Starzl Transplant Institute. We recruited all patients who received a pretransplantation evaluation for KT between March 2010 and October 2012 and prospectively followed the patients and assessed for outcomes until August 2018. Study participants provided informed consent and completed a semistructured telephone interview (≈1 h) after their first KT evaluation appointment. The interview included several previously validated measures[30,31] and was conducted by research interviewers from the Survey Research Program at the University of Pittsburgh Center for Social and Urban Research. We prospectively tracked all participants via medical record through 6-mo post-KT. This article reports on patients who completed a follow-up telephone interview (≈20 min) at ≈6 mo post-KT. See Figure 1 for a visual display of study stages.

We completed the data analysis for this study at the University of New Mexico. It was approved by the Institutional Review Boards at the University of Pittsburgh (PRO09060113) and the University of New Mexico (17-084), and a data use agreement was signed between the 2 institutions. The study was conducted in accordance with the Declaration of Helsinki and is consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Study Sample

Inclusion criteria for this study were (1) age 18 and older; (2) English speaking; (3) referred for KT; (4) underwent KT; and (5) follow-up for ≈6 mo post-KT. Because the majority of US KT recipients are first-time recipients,[32] and to prevent patients' previous experience with KT from influencing current outcomes, we excluded patients if they had a previous KT. Also, we excluded those who had a cognitive or sensory impairment (such as blindness or deafness) that prevented them from completing an interview. Among eligible patients, those enrolled showed no significant differences from those not enrolled on any available demographic characteristics (age, gender, race/ethnicity).[33]

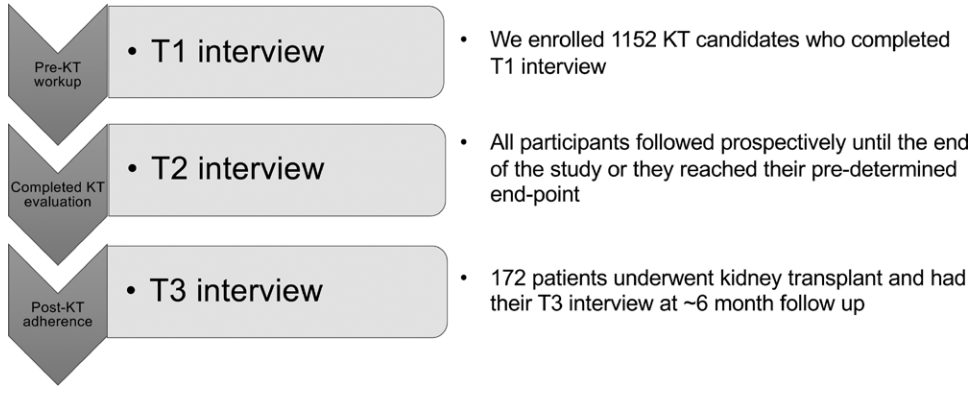

FIGURE 1. Interview time points of study. KT, kidney transplantation; T1, Timepoint 1; T2, Timepoint 2; T3, Timepoint 3.

Potential Predictors

We assessed predictors for nonadherence using the WHO classification of risk factors for nonadherence in chronic disease, and provide extended descriptions, ranges, and psychometric properties in Table 1.

- Sociodemographic factors: race/ethnicity, gender, age, marital status, education, income, and occupation.
- Condition-related factors: dialysis duration, body mass index, and Charlson Comorbidity Index.[35,49]
- Health system/healthcare provider factors: insurance status.

TABLE 1.

Potential predictors[a,b] and transplant adherence outcomes[b]

Predictor categories	Variables	Description	Treatment/range/Cronbach α (if applicable)
Sociodemographic factors			
	Race/ethnicity	1. Non-Hispanic White 2. Non-Hispanic Blacks 3. Others	Categorical, 3 categories
	Gender	Male and female	Dichotomous
	Age	This variable was defined age in years based on interview data and patient-reported date of birth.	Continuous
	Marital status	Reported using the following categories: 1. Single (never married) 2. Separated or Divorced 3. Widowed 4. Married 9. No Answer	Dichotomous; married vs not (all others)
	Education	Reported using the following categories: 1. High school or less 2. Some college 3. College or more	Categorical; 3 categories
	Household income	Reported using the following categories: 1. Under $15 000 2. $15 000–$24 999 3. $25 000–$49 999 4. $50 000–$74 999 5. $75 000–$100 000 6. >$100 000	Categorical; for analysis of this study sample, we trichotomized income as: <$25 000 (low) $25 000–$74 999 (medium) >$75 000 (high)
	Occupation	Classified on a 1–9 scale from (1) Farm Laborers/Menial Service Workers to (9) Higher executives, Proprietors of Large Businesses, and Major Professionals.	Categorical; for this analysis, we classified occupation into "unskilled" (1–3), "skilled" (4–6), and "professional" (7–9)
Condition-related factors			
	Dialysis duration	Time on dialysis (at time of evaluation).	Medical record abstraction; categorical; 3 categories. In this study, because dialysis duration was skewed, we used established literature[34] to determine the following categories for dialysis duration: 1. 0 y on dialysis 2. ≤1 y on dialysis 3. >1 y
	BMI	Calculated with patient height and weight using NHLBI's calculator available at: https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm	Medical record abstraction; continuous
	Charlson Comorbidity Index[35]	Weighted score reflecting the number and severity of comorbid health conditions	Medical record abstraction; continuous; 0 (no comorbidities) to 19 (a higher number of comorbidities or more serious comorbidities)
Health system/healthcare provider factors			
	Insurance status	Insurance status was self-reported using the following categories: 1. Private only 2. Public only 3. Private and Public	Categorical; 3 categories
Patient-related psychosocial factors			
	Experience of racial discrimination[36]	The extent to which a participant experienced a set of discriminatory practices in healthcare settings (eg, "When getting healthcare, I was treated with less respect than other people because of my race or color.").	Categorical; dichotomous; We coded this measure as "any discrimination vs no discrimination"; Cronbach alpha = 0.91
	Perceived racism[37]	Extent to which patients believe that racism is common in healthcare, as opposed to having personal experience with racism in healthcare (eg, "Doctors treat African American and White people the same.").	Continuous; mean score ranging from 1 (strongly disagree) to 5 (strongly agree); Cronbach alpha = 0.746

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TABLE 1. (Continued)

Potential predictors[a,b] and transplant adherence outcomes[b]

Predictor categories	Variables	Description	Treatment/range/Cronbach α (if applicable)
	Medical mistrust[38]	Degree to which participants believe their hospital to be trustworthy, competent, and acting in their best interests (eg, "I trust hospitals").	Continuous; mean score ranging from 1 (strongly disagree) to 5 (strongly agree); Cronbach alpha = 0.844
	Trust in physicians[39]	Degree of patient trust in their physician (eg, "I doubt that my doctor really cares about me as a person").	Continuous; mean score ranging from 1 (totally disagree) to 5 (totally agree). Cronbach alpha = 0.796
	Family loyalty[40]	Feelings of loyalty and mutual support regarding the family (eg, "The family should consult close relatives [uncles, aunts, first cousins] concerning its important decisions".)	Continuous; mean score ranging from 1 (strongly disagree) to 5 (strongly agree). Total score ranges from 8 to 80. Cronbach alpha = 0.802
	Overall religiosity[41]	Religious affiliation and level of importance/influence of religious beliefs (eg, "Regardless of whether you attend religious services, please indicate on a scale from 1 [not at all] to 9 [extremely] how important your religious beliefs are to you.")	Continuous; mean score ranging from 1 (not at all) to 9 (extremely). Cronbach alpha = 0.912
	Perceived burden of kidney disease[42]	Participants rated the extent to which they felt burdened by their kidney disease (eg, "My kidney disease interferes with my life").	Continuous; mean score ranging from 1 (definitely true) to 5 (definitely false); Cronbach alpha for the current sample = 0.772
	Social support[43]	ISEL-12 assesses patients' perceived availability of 3 separate functions of social support: tangible, appraisal, and belonging (eg, "I feel that there is no one I can share my most private worries and fears with").	Continuous; score ranging from 1 (definitely false) to 4 (definitely true) for each item; total score range = 12–48. Cronbach alpha = 0.850
	Self-esteem[44]	Rosenberg Self-Esteem Scale assesses patients' feelings of self-worth and self-respect (eg, "I feel that I am a person of worth, at least on an equal plane with others").	Continuous; mean score ranging from 1 (strongly agree) to 4 (strongly disagree). Cronbach alpha = 0.852
	Sense of mastery[45]	Sense of Mastery Scale[45] assess the degree to which participants feel they have personal control over the things that happen to them (eg, "I have little control over the things that happen to me.")	Continuous; mean score ranging from 1 (strongly agree) to 4 (strongly disagree). Cronbach alpha = 0.803
	Locus of control[46]	18-item MHLC scales, Form C, assessed the extent to which recipients view their health condition is due to their own behavior (Internal Locus of Control) or the behavior of doctors, other people not including doctors, chance, luck, or fate (External Locus of Control).	Continuous; mean score ranging from 1 (strongly disagree) to 6 (strongly agree). Cronbach alpha = 0.760 for Internal Locus of Control Cronbach alpha = 0.813 for External Locus of Control
	Anxiety[47]	Anxiety subscale of the BSI (eg, "nervousness or shakiness inside".)	Continuous; mean score ranging from 1 (not at all) to 5 (extremely); Cronbach alpha = 0.82
	Depression[47]	Depression subscale of the BSI (eg, "feeling hopeless about the future".)	Continuous; mean score ranging from 1 (not at all) to 5 (extremely); Cronbach alpha = 0.82
	Transplant knowledge[42,48]	KT Knowledge Survey and the KT Questionnaire. This measure includes 27 multiple choice and true-false items. A summative score was created for the total number of items that patients answered correctly.	Continuous; total score ranging from 0 (less transplant knowledge) to 27 (more transplant knowledge)
	Transplant learning activities	Type, number, and time spent in each educational activity were assessed by self-report (eg, "Read brochures about kidney transplant from living donors"). We calculated a summative score for the total number of items checked and total time spent on all learning activities.	Continuous; total activities ranging from 0 to 8 learning activities

Adherence outcome measures

Outcomes	Measurements	Description
Medication adherence	"How often would you say you have missed taking this medication?" 1 = Every day 2 = Several times a week 3 = About once a week 4 = Several times a month 5 = About once a month 6 = Less often than once a month 7 = Never	For medication adherence, we calculated the composite score as the average of the individual scores for calcineurin inhibitors, antimetabolite, prednisone, and antihypertensives. Lower score indicated lower adherence and a higher score indicating greater adherence. For example, if a patient reported never missing his calcineurin inhibitor (7), but missed his antimetabolite and steroids less often than once a mo (6) and his antihypertensives several times a mo (4), his composite score for medication adherence would be 5.75 ([7+6+6+4]/4 = 5.75).

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TABLE 1. (Continued)

Potential predictors[a,b] and transplant adherence outcomes[b]

Predictor categories	Variables	Description	Treatment/range/Cronbach α (if applicable)
Healthcare follow-up		"Have you had to cancel or reschedule appointments/lab test? Would you say that has happened:" 1 = Frequently 2 = Occasionally 3 = Never	106 patients reported never canceling or rescheduling an appointment or a lab test and 67 patients reporting occasionally missing any clinic appointments or laboratory testing. No patient reported frequent cancelation of an appointment and only 2 patients reported frequent rescheduling a lab test. Therefore, we dichotomized this outcome into ever (0) vs never (1) missing any clinic appointments or laboratory testing.
Lifestyle recommendations			
Blood pressure measurement		"How often do you check your blood pressure?" 1 = Never 2 = Less often than once a month 3 = About once a month 4 = Several times a month 5 = About once a week 6 = Several times a week 7 = Every day	Due to the poor internal consistency among the individual items in the lifestyle domain, we were unable to use a composite score for this domain. Thus, to reduce false-positive discoveries, we focused on the 2 most clinically relevant outcomes in lifestyle behavior post-KT—diet and exercise.
Dietary recommendations		"How often do you go off your diet?" 1 = Every day 2 = Several times a week 3 = About once a week 4 = Several times a month 5 = About once a month 6 = Less often than once a month 7 = Never	
Exercise		"How often in a typical month do you exercise (ie, perform a regular program of exercise beyond daily chores)?" 1 = Never 2 = Less often than once a month 3 = About once a month 4 = Several times a month 5 = About once a week 6 = Several times a week 7 = Every day	
Smoking		"Since the transplant, have you smoked cigarettes?" 1 = Yes, more than 1 pack per day, on average 2 = Yes, 11–20, cigarettes per day (1 pack), on average 3 = Yes, 1–10 cigarettes per day (½ pack), on average 4 = Yes, not every day 5 = Never	
Alcohol		"How often do you *usually* have any alcohol (either wine, beer, hard liquor, coolers, etc)." 1 = ≥3× a day 2 = 2× a day 3 = About once a day 4 = Nearly every day (5–6× a week) 5 = 3× or 4× a week 6 = Once or twice a week 7 = 2× or 3× a month 8 = About once a month 9 = Less than once a month, but at least once a year 10 = Less than once a year 11 = Never	

[a]We included these measures because they (1) are widely used in organ donation and/or transplantation studies, other medical populations, or both; (b) have known psychometric properties, including (for scaled measures) Cronbach αs of ≈0.80–0.92 (see references cited with each instrument for psychometric data); and (3) used in our previous research.
[b]All patient self-report unless otherwise specified.
BMI, body mass index; BSI, Brief Symptom Inventory; ISEL, Interpersonal Support Evaluation List; KT, kidney transplantation; MHLC, Multidimensional Health Locus of Control; NHLBI, National Heart, Lung, and Blood Institute.

- Patient-related psychosocial factors: experience of race-based discrimination,[36,50,51] perceived racism,[37,52] medical mistrust,[37,38,52] trust in physicians,[39] perceived burden of kidney disease,[42,48] emotional distress (anxiety and depression),[47] social support,[43,53] self-esteem,[44] sense of mastery,[45] locus of control,[46] family loyalty,[40] overall religiosity.[41] transplant knowledge,[42,48,54] and transplant learning activities.

- Treatment-related factors: not included in this study as our aim was to examine pre-KT factors that predicted post-KT adherence.

Outcome Variables

Our primary outcome variables were post-KT adherence measured in 3 different domains at ~6 mo post-KT. We assessed adherence in each domain using the Health Habit Survey questionnaire that has been validated in many previous studies of adherence in organ transplantation.[18,55-57] The Health Habit Survey uses patient self-report measures on adherence of each individual health habit including adherence to medication, clinic appointments, diet, exercise, home blood pressure monitoring, smoking, and alcohol consumption. We used self-report measures because they are commonly used, easy to implement, yield rates of nonadherence as good as or better than other adherence measures, and correlate with other adherence measures.[18,58-61]

For this study, we measured 3 different domains of adherence: medication, healthcare follow-up, and lifestyle behaviors. Because there is no uniform definition/cutoff for many adherence outcomes including medication or lifestyle behavior, we assessed adherence as an approximately continuous variable when appropriate, with a higher score indicating more frequent engagement in the behavior rather than an all-or-none behavior. Because our goal was to determine whether variables assessed at KT evaluation would predict whole classes of nonadherence behaviors (eg, assessing adherence to medication as a group rather than adherence to individual medication such as calcineurin inhibitors or antimetabolites), we computed a composite score for each domain of adherence (see Table 1 for measurement and calculation details) when internal consistency between the individual items in a domain of adherence (Cronbach alpha) was acceptable. We assessed the internal consistency of individual items in each domain and found acceptable levels in medication and healthcare follow-up. As a result, we used composite scores of Likert scale items in those 2 domains. Due to poor internal consistency among the individual items in the lifestyle domain, we were unable to use a composite score for this domain. Thus, to reduce false-positive discoveries, we focused on the 2 most clinically relevant outcomes in lifestyle behavior post-KT, diet and exercise.[62-65]

1. Medication: frequency at which patients missed their medications (immunosuppressants and antihypertensive medications).
2. Healthcare follow-up: frequency at which patients missed their clinic appointments and/or laboratory tests.
3. Lifestyle behavior for kidney transplant recipients: frequency with which patients engage in lifestyle behavior, including dietary recommendations or exercise.

Statistical Analysis

We examined baseline characteristics using mean and SD for continuous variables and count with percentage for categorical variables. To assess how baseline characteristics were associated with adherence outcomes, we built multiple linear regression models for medication and lifestyle recommendations adherence (continuous outcomes) and logistic regression for healthcare follow-up adherence (dichotomous outcome). We selected covariates that were potentially associated with the outcomes in pairwise analyses into the adjusted linear and logistic regression models. To base our variable selection on statistical significance and clinical meaningfulness, for the continuous outcomes, our inclusion criteria required both (1) a P value from tests ≤0.20 for all variables and (2) either a Kruskal–Wallis test statistics of ≤−1.50 or ≥1.50 for a categorical predictor or a Spearman correlation of ≤−0.2 or ≥0.2 for a continuous predictor. For the dichotomous outcome, our inclusion criteria required both a (1) P value from tests ≤0.20 for all variables and (2) either a Kruskal–Wallis test statistic ≤−1.50 or ≥1.50 for a continuous predictor or an odds ratio (OR) of ≤0.50 or ≥2.0 for a categorical predictor. Upon fitting regression models with covariates meeting our inclusion criteria, we applied False Discovery Rate adjustment to maintain the overall false positive rate to be within the nominal level (0.05).

Given varying definitions of nonadherence[66] in the literature and that most of the literature reported medication adherence as a dichotomous outcome, we performed a supplementary comparison analysis of dichotomized medication nonadherence (defined as missing medications more or less frequently than once a mo).[55] As this outcome was dichotomized, we used the criteria above for logistic regression analysis. In addition, we noted that more than half of our patients underwent live donor KT (LDKT). To assess if our findings would differ between those who had undergone LDKT versus deceased donor KT, we performed sensitivity analyses by including type of transplant as a covariate in our models. Please see **Appendix 1** (**SDC**, http://links.lww.com/TXD/A394) for variable selection in the univariate models. We performed all data analyses using R statistical software (version 3.5.3).

RESULTS

A total of 1726 KT candidates were initially referred to University of Pittsburgh Medical Center for KT evaluation. In Figure 2, we show that 1152 candidates were seen in KT evaluation clinic, consented, and followed prospectively. At the end of the study period, all 173 candidates who underwent KT at our institution and had ~6 mo follow-up, were included in this paper. The mean time from KT evaluation to KT was 1.78 ± 0.87 y.

Baseline Characteristics

Of the 173 participants, 80% were White, 61% had at least some college education, and 75% had an annual household income ≥$25 000. Half of the study population was male and had only private insurance. At the time of their initial evaluation for transplant, most of the patients had minimal dialysis exposure—92 patients (53%) had never been on dialysis, and 48 patients (28%) had been on dialysis for less than a year (Table 2). We included details of other baseline factors and nonadherence outcomes in Table 2.

Adherence Outcomes

Before statistical modeling, we assessed for multicollinearity by computing correlation coefficients and multivariable variance inflation factors for all variables of interest. We identified no major concerns. Internal consistency was highest for medical adherence (Cronbach alpha = 0.82), lower for healthcare follow-up (alpha = 0.34), and poor for lifestyle adherence

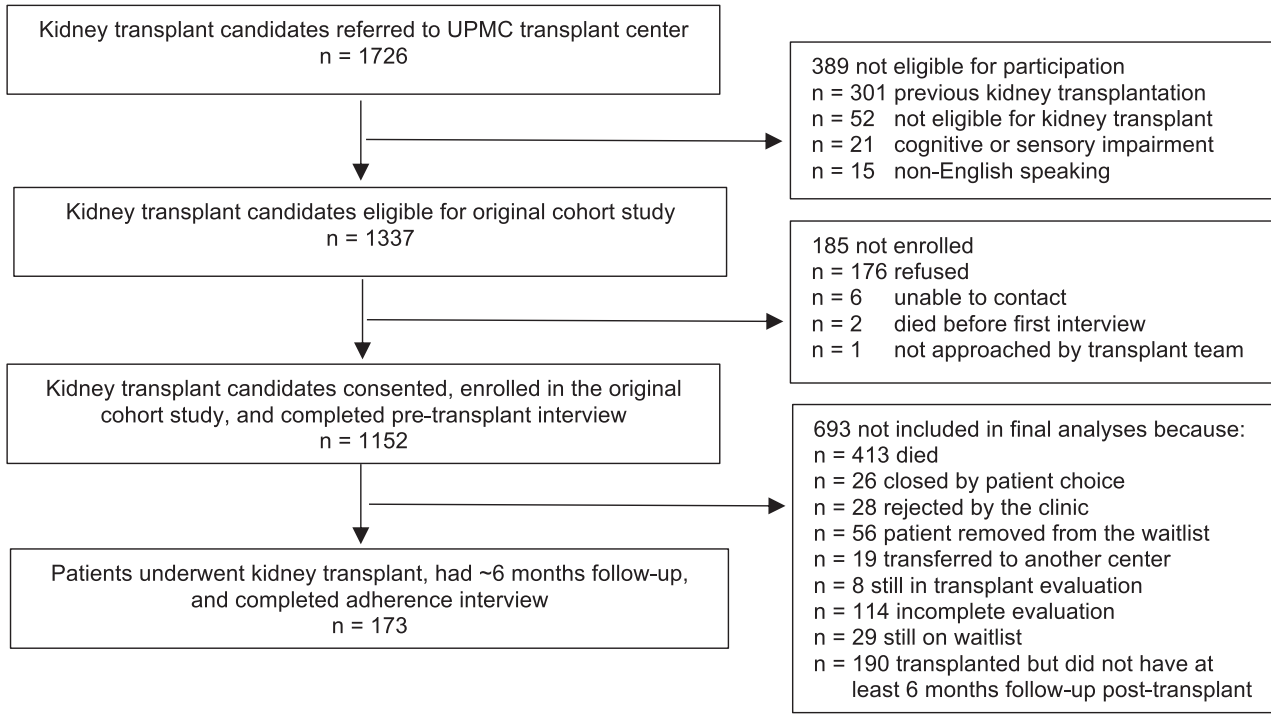

FIGURE 2. Kidney transplant candidates included and excluded from study cohort. UPMC, University of Pittsburgh Medical Center.

(alpha = 0.10). In the adjusted linear regression model of medication adherence post-KT (Figure 3A), we found that Black patients had lower medication adherence than White patients with a mean adherence score difference of −0.72 (95% confidence interval [CI], −1.12 to −0.32) on a 7-point scale. The highest income group had lower adherence than the lowest income group (mean adherence score difference, −0.34; 95% CI, −0.67 to −0.02). When we analyzed the dichotomized medication adherence (see **Appendix 2** [**SDC**, http://links.lww.com/TXD/A394]), both Black race (OR, 0.17; 95% CI, 0.05–0.58) and higher income (OR, 0.15; 95% CI, 0.04–0.52) remained predictors of lower medication adherence.

Our adjusted logistic regression model predicting the probability of adherence to healthcare follow-up (including clinic appointments and laboratory testing, Figure 3B) showed that patients who reported experiencing any racial discrimination had lower odds of adherence to healthcare follow-up compared to patients who reported no experience of racial discrimination (OR, 0.31; 95% CI, 0.12–0.76). Patients with a stronger internal locus of control had higher odds of adherence to healthcare follow-up (OR, 1.46; 95% CI, 1.06–2.03).

In the lifestyle domain, our adjusted linear regression model for dietary recommendations (Figure 3C) showed that patients with higher education level (college or more) had better adherence than those with lower education level (high school or less) (mean adherence score difference, 0.75; 95% CI, 0.21–1.29) on a 7-point scale, and body mass index (BMI) was negatively associated with adherence to dietary recommendations (mean adherence score difference for every unit increase in BMI: −0.08; 95% CI, −0.03 to −0.13). Our multiple linear regression model did not identify any statistically significant predictors (Figure 3D) of exercise adherence.

We found that patients who adhere to medications were more likely to adhere to healthcare follow-up. The odds ratio of never missing an appointment or a lab test was 1.66-fold (95% CI, 1.11–2.47; P = 0.013) as high with every 1-point increase of medication adherence score. Median medication adherence score was 7.00 among those who never missed an appointment or a lab test versus 6.25 among those who ever missed an appointment or lab test (Kruskal test P = 0.003).

In our sensitivity analyses examining type of transplant, type of transplant was not significantly associated with medication adherence or any of the lifestyle adherence. Type of transplant was associated with adherence to healthcare follow-up with patients who underwent LDKT having lower adherence to healthcare follow-up (OR, 0.45; 95% CI, 0.22–0.9).

DISCUSSION

In this study, we tracked prospectively how pre-KT baseline socio-demographics, condition-related, health system/healthcare provider and patient psychosocial factors predict post-KT nonadherence behaviors in three separate domains concurrently. This timing is important because it may allow transplant teams to target patients who would benefit from adherence intervention both pretransplant and early posttransplant. The prospective collection of data and chart reviews resulted in an abundant amount of data available to test for potential risk factors that may predict post-KT nonadherence.

Although there have been papers that have examined multiple adherence outcomes in the kidney transplant population, including 2 meta-analyses, one in the pediatric and the other in the adult population,[14,18] as well as a recently published cross-sectional study by Sanders-Pinheiro et al,[67] our study is unique in that we studied all 3 adherence outcomes in a kidney transplant patient sample prospectively in a single study. We believe that studying all 3 outcomes concurrently in the same population is important as they all may contribute to poor allograft outcomes. Using the same population allowed

TABLE 2.

Baseline characteristics and outcome variables

Variables	Total N = 173	
Demographics factors; n (%)		
Race		
NH White	139	(80.40)
NH Black	18	(10.40)
Other	16	(9.20)
Gender		
Male	98	(56.60)
Female	75	(43.40)
Age; m (SD)	51.10	(17.70)
Education		
High school or less	68	(39.30)
Some college	45	(26.00)
College or more	60	(34.70)
Occupation		
Unskilled	41	(23.70)
Skilled	68	(39.30)
Professionals	64	(37.00)
Household income		
<$25 000	42	(25.30)
$25 000–$74 999	77	(46.40)
≥$75 000	47	(28.30)
Insurance		
Public only	33	(19.20)
Mixed	55	(32.00)
Private only	84	(48.80)
Marital status		
Married	105	(60.70)
Not married	68	(39.30)
Medical/health factors		
Charlson Comorbidity Index; m (SD)	3.59	(1.45)
BMI; m (SD)	27.99	(5.71)
Burden of kidney disease; m (SD)	3.42	(1.10)
Dialysis duration (y); n (%)		
0	92	(53.20)
≤1	48	(27.70)
>1	33	(19.10)
Culturally related factors		
Experienced discrimination in healthcare; n (%)		
No	146	(84.40)
Yes	27	(15.60)
Overall religiosity (1 = not at all; 9 = extremely); m (SD)	5.66	(2.67)
Racism in healthcare (1 = strongly disagree; 5 = strongly agree); m (SD)	2.29	(0.69)
Medical mistrust (1 = strongly disagree; 5 = strongly agree); m (SD)	2.36	(0.46)
Trust in physician (1 = totally disagree; 5 = totally agree); m (SD)	2.15	(0.50)
Family loyalty (total score range from 8 to 80); m (SD)	48.37	(9.49)
Psychosocial characteristics; m (SD)		
Social support (total score range from 12 to 48)	44.13	(4.65)
Self-esteem (1 = strongly disagree; 4 = strongly agree)	3.23	(0.45)
Mastery (1 = strongly disagree; 4 = strongly agree)	3.03	(0.36)
Internal locus of control (1 = strongly disagree; 6 = strongly agree)	3.69	(1.10)
External locus of control (1 = strongly disagree; 6 = strongly agree)	3.20	(0.70)
Anxiety (1 = not at all; 5 = extremely)	1.40	(0.54)
Depression (1 = not at all; 5 = extremely)	1.33	(0.49)
Transplant-related beliefs; m (SD)		
Transplant knowledge (scale: 0–27)	22.43	(2.22)
Number of learning activities	5.06	(1.40)
Adherence outcomes		
Medication (scale: 1–7; higher number = better adherence); m (SD)	6.37	(0.81)
Medication; n (%) (dichotomous)		
Adherent	136	(78.60)
Nonadherent	37	(21.40)
Appointment cancelation (clinic appointments, lab testing); n (%)		
Adherent	106	(61.27)
Nonadherent	67	(38.73)
Diet (scale: 1–7; higher number = better adherence); m (SD)	5.43	(1.77)
Exercise (scale 1–7: higher number = better adherence); m (SD)	4.10	(1.99)

n missing: income = 7; insurance = 1; religiosity = 1; racism = 2; exercise = 1; diet = 14.
BMI, body mass index; m, mean; n, number; NH, non-Hispanic.

Continued next page

us to address the question of whether the at-risk population for one domain of nonadherence is the same as the at-risk population for other domains. We found that Black race and higher income were associated with lower medication adherence. Experience of racial discrimination in healthcare or a low internal locus of control each predicted poorer adherence to healthcare follow-up. Having a lower education or higher BMI each predicted lower adherence to dietary recommendations. Our findings suggest that the at-risk population for one domain of nonadherence may not be the same as those at risk for other nonadherence behaviors, which is consistent with the findings and conclusions from the meta-analyses by Dew et al.[18] Thus, individualizing strategies to target the different populations who are at risk for different nonadherence behaviors both pre-KT and early post-KT may improve adherence behaviors post-KT in the respective domains.

Dew et al[18] showed that nonadherence rates and risk factors differed by the outcomes assessed (medication nonadherence, healthcare requirements, and lifestyle recommendations). However, the authors were not able to adequately assess the effect of cultural and psychosocial factors on nonadherence outcomes. Although there have been studies looking at the effect of different nonmedical factors on nonadherence outcomes in KT, namely medication nonadherence,[22,28,68-71] they were limited to cross-sectional analyses. None have focused on assessing these variables pre-KT, especially the effect of racial discrimination and medical mistrust, and using them to predict post-KT nonadherence. In addition, few studies looked at other nonadherence outcomes, such as healthcare requirements or lifestyle recommendations, especially concurrently.

Our finding that Black race was associated with lower medication adherence confirms previous findings that Black race is a risk factor for medication nonadherence,[25,70,72] although a successful intervention to weaken this association is still lacking. Considering our work in light of the findings of Taber et al[4] and Goodall et al,[5] who showed that patients who frequently missed clinic appointments have worse clinical outcomes, our study suggests the importance of examining a

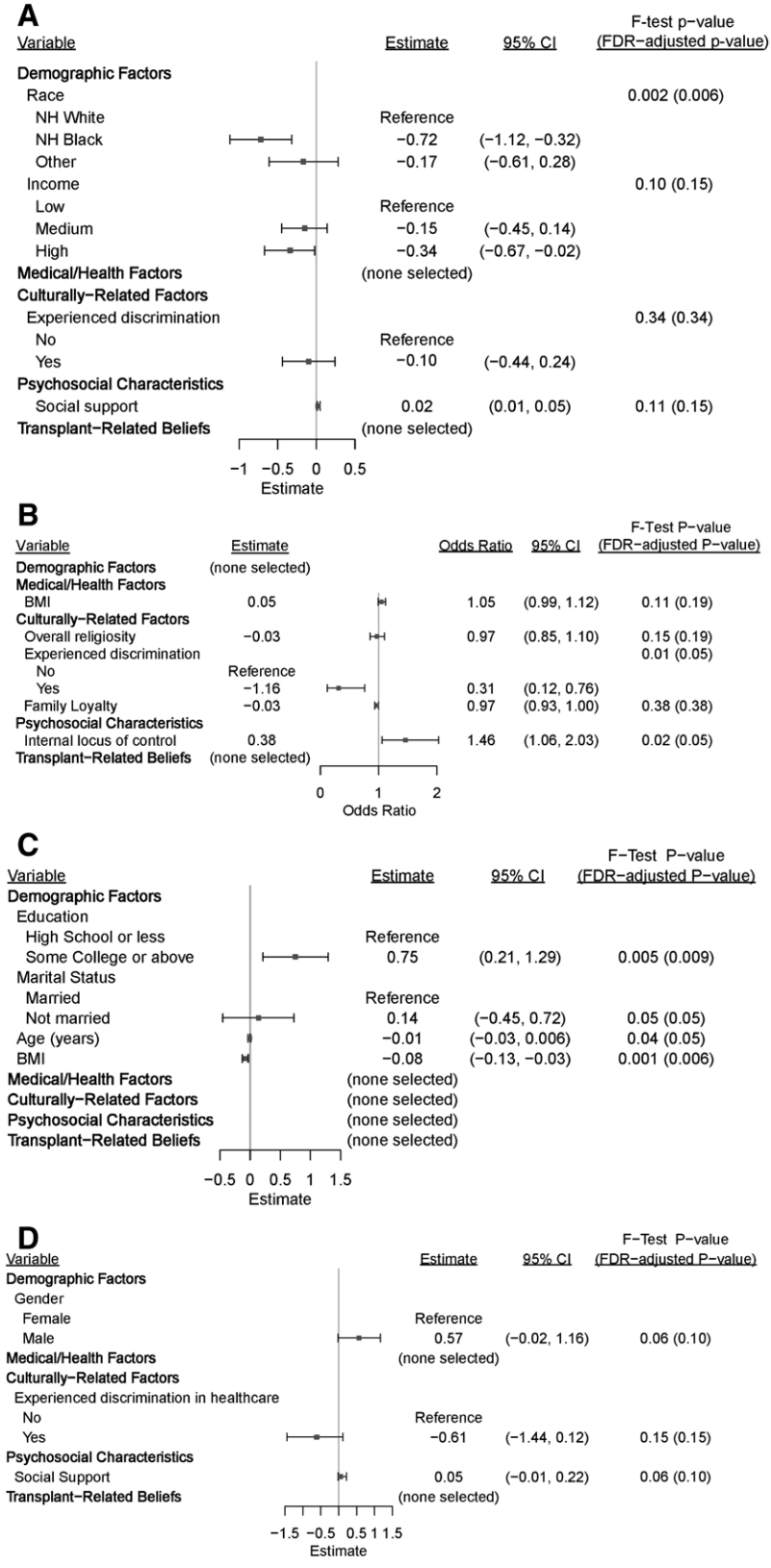

FIGURE 3. Baseline factors associated with adherence outcomes. BMI, body mass index; CI, confidence interval; FDR, False Discovery Rate; NH, non-Hispanic.

variety of nonadherence outcomes rather than focusing solely on medication nonadherence. Our finding that Black race and experience of racial discrimination predicted lower adherence suggests that patients may forego medical recommendations from their provider due to previous unpleasant experiences. Such results may highlight the need for strategies to reduce systemic racism as well as implementation of further cultural sensitivity training and reduction in unconscious biases

among healthcare workers to improve patient experiences. In addition, culturally sensitive education material for patients as well as reduction in dosing frequency of medication for patients at risk for nonadherence may help reduce the risk of nonadherence.

We found that lower education and higher BMI are both associated with lower adherence to dietary recommendations. This result is consistent with findings from Hedayati et al[7] who showed in their study that patients with lower social support and education levels have lower adherence to lifestyle recommendations. Social determinants of health are well-known risk factors for access to kidney transplant,[33,73] and our study suggests that such factors may play a role in post-KT care as well. Identifying these patients early in the process may allow the transplant team to intervene by providing better education and formulating better dietary habits pre-KT and early post-KT to combat posttransplant complications such as weight gain.

Our finding that higher income was associated with lower medication adherence was unexpected. A literature search yielded only 1 article by Marsicano et al,[74] showing that patients with higher income had lower medication adherence. The study was conducted in Brazil where lower-income patients had better access to care and healthcare cost coverage, which is not the case here in the United States. Thus, the speculated cause for this association is unlikely to be the same. In this study, we ended up with a sample of patients with a higher proportion who underwent LDKT compared with national data. LDKT recipients are known to have a higher risk for nonadherence.[25,75,76] We speculate that this association may have been unique to this single-center study sample. This finding will need to be confirmed in larger multicenter trials in the future.

The dearth of literature assessing domains other than medication nonadherence highlights the need for larger, multicenter studies to develop strategies to address nonadherence behaviors in various domains. For this study, we analyzed adherence as a continuous outcome variable when appropriate (higher score indicating more frequent engagement in the defined activity) rather than a dichotomous outcome (ie, adherent versus nonadherent) due to the lack of widely accepted standardized cutoff for adherence whether it is in adherence to medication, healthcare follow-up, or lifestyle behavior. Our sensitivity analysis using dichotomized medication adherence showed similar results. Currently, there is a lack of international consensus on the optimal methods used to assess nonadherence (eg, self-report versus drug levels versus pharmacy refill history[18]) as well as the cutoff to dichotomize adherence versus nonadherence. Cutoffs used are often arbitrary and of no clinical significance.[25,77] Measuring adherence using a continuous scale based on patient's self-report of medication nonadherence may overcome the need for clinicians to label their patients as adherent versus nonadherent. Clinicians are skilled at identifying patients who are overtly nonadherent but have been shown to overestimate their patients' adherence.[59,77,78]

The results of our study should be interpreted in light of some limitations. First, many of the variables and outcome measures were self-reported, for example, education, income, insurance as well as adherence outcomes, and may be subject to patient bias. This shortcoming is inherent to all studies using patient-reported variables. However, we have attempted to improve the validity of our self-report outcome measures, especially our adherence outcomes, by normalizing nonadherence and ensuring that the staff administering the survey was different from the healthcare team to minimize the effect of social desirability.[58] Second, this was a single-center study. More than 50% of our study sample underwent LDKT, which is not reflective of the general KT population. Organ procurement and transplantation network data in 2019 showed that 62% of kidney transplants in the United States were from deceased donors.[79] The high rate of LDKT and the high percentage of patients who were not on dialysis at the time of kidney transplantation evaluation suggest that this may be a unique sample. We addressed this shortcoming by including the type of transplant in our sensitivity analyses and found that type of transplant only affected adherence to healthcare follow-up. Furthermore, our study did not have adequate power to incorporate the complex interactive relationship between income, age, and insurance into our models, despite signs of potential confounding between them. The limitations of our small single-center study and the small number of minority population including Black individuals and other minorities argue for the need for larger prospective multicenter studies to replicate our findings and investigate the complex association between pre-KT risk factors and post-KT adherence outcomes. Finally, in this study, we did not assess the association of adherence outcomes with subsequent clinical outcomes including allograft failure, rejection, and death. Given our short follow-up period, such an analysis was beyond the scope of the current study.

CONCLUSION AND IMPLICATIONS

In this study, we showed that different risk factors predicted different adherence outcomes. The examination of these variables and timing of assessing predictors and outcomes is important because it could help clinicians identify patients who are at high risk for nonadherence early in the transplant evaluation process so that interventions can be initiated earlier—either pre- or early post-KT. In line with Nevin et al's[80] findings that patients with early posttransplant nonadherence had worse clinical outcomes, early identification of risk is critical to long-term success. Thus, we recommend that transplant teams individualize strategies to target different at-risk populations when trying to address specific nonadherence behaviors. This approach may enable clinical teams to intervene with at-risk patients pre-KT and immediately post-KT to enhance their adherence, thereby improving long-term graft survival and patient outcomes.

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