ORIGINAL ARTICLE

The prevalence, risk factors, and outcomes of medication trade-offs in kidney and liver transplant recipients: a pilot study

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SUMMARY

High out-of-pocket medication costs negatively impact adherence in transplantation. We evaluated the association of "medication trade-offs"—defined as choosing to spend money on other expenses over medications—with medication nonadherence and transplant outcomes. From 2011 to 2012, we performed a prospective study of 201 transplanted recipients ($n = 103$ liver, $n = 98$ kidney and) at two large US transplant centers. Structured interviews assessed socio-demographics, medication adherence, and medication trade-offs. Multivariable models assessing risk factors for medications trade-offs and the association between medications trade-offs and post-transplant hospital admissions were performed. A total of 17% of patients reported medication trade-offs; the most common trade-offs were inability to afford a prescription in the past 12 months and making choices between prescriptions and food. In multivariable analysis, insurance type (RR: 2.97, 95% CI: 1.19–7.40), limited health literacy (RR: 2.64, 95% CI: 1.23–5.64), and ≥3 comorbid conditions (RR: 2.48, 95% CI: 1.09–5.62; all $P < 0.05$) were associated with trade-offs. Patients with trade-offs were more likely to report nonadherence to medications (mean adherence: 77 ± 23% with trade-offs vs. 89 ± 19% without trade-offs, $P < 0.01$). The presence of medication trade-offs was associated with post-transplant hospital admissions (RR 1.64, 95% CI 1.14–2.35, $P < 0.01$). Assessments of financial barriers are warranted in clinical practice to identify nonadherence and improve post-transplant outcomes.

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Key words
financial barriers, kidney transplant, liver transplant, medication nonadherence, outcomes

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Introduction

Prescription medication costs are the fastest growing segment of healthcare expenditures in the United States [1–3]. To mitigate insurance payer spending increases on prescription medications over the last 15 years, medication copayments (i.e., out of pocket spending) spending on medications (i.e., cost sharing) have risen in parallel. Previous literature has shown that increased cost sharing has led to unintended adverse consequences such as decreased essential medication adherence, more frequent emergency department visits, admissions to hospitals and long-term health facilities, and increased mortality [3,4]. According to a recent Kaiser Health Tracking Poll, the top two healthcare issues reported by Americans were the need to expand the availability of highly essential, expensive medications and to reduce prescription drug prices [5].

Similar to the general chronic disease population, cost concerns and cost-related medication nonadherence are commonly reported by transplant practitioners and patients [6,7]. A study by Woodward *et al.* [8,9] showed that loss of Medicare coverage in kidney transplant (KT) recipients was associated with graft loss and that extending Medicare coverage (including prescription benefits) from 1 to 3 years largely benefited low-income recipients who were presumably more sensitive to cost sharing. Medication nonadherence rates among solid organ transplanted recipients mirror those of the general population with most studies reporting a 30–50% prevalence, however, with some studies reporting up to 50–80% [10–14]. Among KT recipients, an estimated 12–15% of allograft losses are due to medication nonadherence; however, the role of nonadherence in allograft failure in liver transplantation is not as well described [15,16]. To date, no published studies have assessed how often transplanted recipients make choices between taking their medications and other expenses and how these choices affect medication nonadherence and post-transplant clinical outcomes.

The objectives of this study were to evaluate risk factors for liver and kidney transplanted recipients having "medication trade-offs," defined as making choices between spending money on medications versus other essential expenses, and whether the presence of medication trade-offs was associated with nonadherence and adverse post-transplant outcomes. We hypothesized that the prevalence of medication trade-offs would be similar across groups; however, kidney transplanted recipients would experience more financial barriers to adherence more than 3 years after transplantation due to loss of Medicare prescription coverage.

Patients and methods

Study procedure

Between 2011 and 2012, at two academic medical centers in Chicago, IL, and Atlanta, GA, we conducted a prospective study of prevalent LT and KT recipients ages 18 and older. Patients were identified via convenience sampling as they came for routine transplant follow-up appointments. Participants underwent structured, in-person interviews that took place during outpatient post-transplant appointments. Recipients >30 days post-transplant were included. Patients were excluded if they had limited English proficiency or severe hearing, vision, or cognitive impairment precluding study participation. Interviews were conducted by trained research coordinators to assess demographics, health literacy, cognitive function, social support, self-reported medical comorbidities, current medications, insurance coverage, pharmacy information, and total monthly copays. The primary exposure, the presence of a medication trade-off, was assessed using a 4-item, previously validated questionnaire (see Exposures). All participants signed written informed consent forms on the interview day. The Institutional Review Boards at both sites approved study protocols and procedures. Participation rates were calculated using the American Association for Public Opinion Research Standards [17].

Exposures

The primary exposure of interest, medication trade-offs, was assessed by asking patients the following four questions adapted from the US Department of Agriculture Food Insecurity Questionnaire (Table 2): "(i) Have you needed a prescription but could not afford it in the past 12 months, (ii) Put off paying for a prescription to buy food, (iii) Spaced out the frequency of your prescription due to cost, (iv) Had to make a choice between buying a prescription or buying food" [18]. Participants who answered "yes" to any of the questions were scored as having a medication trade-off. Trade-offs were analyzed as binary yes/no variable as well as a three-level categorical variable (no trade-offs/at least one trade-off/two or more trade-offs). The brief questionnaires were interviewer-administered and took less than 1 minute to complete.

All participants were asked general socio-demographic questions, including annual household income. Health literacy was assessed using a brief and validated scale, the Newest Vital Sign (NVS); a score of <4 was considered to be less than adequate literacy [19]. Global cognitive

function was measured by the Mini-Mental State Examination (MMSE); a score of <24 was considered to be cognitive impairment [20]. Social support was measured using the 6-item Lubben Social Network scale; <12 was scored as low social support [21]. The NVS, MMSE, and Lubben scores were converted to binary exposures. Participants were asked to bring all medications to the study visit, if not available, the most updated medication list from the electronic medical record was used to record medication data. Each medication was recorded by the research coordinator. Self-reported medication adherence was assessed for each medication using the Patient Medication Adherence Questionnaire (PMAQ) [22]. Patients were considered nonadherent if they reported having missed a dose of any of their transplant or chronic disease medications in the past 4 days. An overall mean adherence score was calculated for each participant by dividing the number of adherent medications by the total number of medications and converted to a percentage. Transplant medications were considered to be immunosuppression regimens (calcineurin and mTOR inhibitors, antimetabolites, steroids) and medications to prevent infection (nystatin, acyclovir, etc.). Chronic disease medications included all other medications excluding multivitamins, supplements, short-term prescriptions such as antibiotics and injectables (e.g., insulin). Participants were additionally asked about the type of pharmacy they used and information regarding insurance coverage (e.g., Medicare, commercial insurance, self-pay). Clinical data such as time since transplant and hospital admissions were abstracted from the electronic medical record (EMR) by trained research coordinators at both sites.

Outcomes

Post-transplant hospital admissions that occurred for up to 12 months after the interview were recorded from the EMR. Admissions at hospitals outside of the transplant center were also recorded whenever possible by reviewing post-transplant care coordination notes. Hospital admission was treated as a binary outcome. Additional outcomes included biopsy-proven rejection episodes and infections as abstracted from the medical record for 12 months following the interview. Clinical follow-up data also included death data for 12 months following the interview.

Statistical analysis

Continuous variables were compared between recipients who did and did not report medication trade-offs using *t*-tests for normally distributed variables and using rank sum tests for non-normally distributed variables. Categorical variables were compared between groups using chi-squared or Fisher's exact tests, as appropriate. A modified multivariable Poisson regression with robust error variance was used to estimate the relative risk of factors associated with medication trade-offs and post-transplant hospital admission. Poisson regression was chosen instead of logistic regression, because logistic regression analysis may result in odds ratios that overestimate relative risks when an outcome is common, as was the case in this study [23]. In the multivariable model for the outcome of medication trade-offs, covariates were purposefully selected using socio-demographic variables, including income, time from transplant, clinical variables, which were deemed biologically plausible to affect the outcome, and those with $P < 0.10$ in univariable analyses. Forward and backward elimination procedures were subsequently carried out to improve model fit. A similar variable selection approach was used for the outcome of post-transplant hospital admissions (univariable results guiding variable selection for the outcome of post-transplant hospital admissions are reported in the Table S2). Multicollinearity testing of covariates was performed for all models and indicated low levels of multicollinearity (largest variance inflation factor: 1.67) [24]. All variables were assessed for missing data and were >99% complete with exception of self-reported income, which was 95% complete. Differences in medication trade-offs and hospital admissions between patients with missing income data and the rest of the study sample were assessed. There were no differences for the main outcomes of medication trade-offs ($P = 0.17$) or hospital admissions when comparing patients with missing income data to the rest of the study sample ($P = 0.47$). Analyses were performed using STATA 13 (Stata Corporation, College Station, TX, USA).

Results

A total of 407 individuals were contacted to participate in the study prior to the visit; two were deceased, 16 were ineligible (12 due to limited English proficiency and four for severe cognitive/hearing impairment), 145 refused and 40 initially agreed, but could not be interviewed due to scheduling conflicts. The final study sample consisted of 201 participants (103 LT, 99 KT) with an overall cooperation rate of 58 percent calculated from among the 347 eligible patients who were available for interviews [12]. There were no significant differences in age, gender, race/ethnicity, or time since transplant

between patients who participated versus those that opted out of the study. However, KT recipients were more likely to have refused participation compared to LT recipients (60% vs. 40%, $P = 0.04$, Table S1).

Overall, 34 (17%) of transplanted recipients had a medication trade-off. Table 1 contains the socio-demographic, psychosocial, and clinical characteristics of the study sample, stratified by the presence of a medication trade-off. The mean age of the study sample was 55 (SD = 13) years with the majority of patients in the 46–64 age group. In univariate analyses, patients ages 31–45 and 46–54 years of age were more likely to report medication trade-offs than those younger than 31 or 65 and older (71% vs. 51%, $P = 0.02$). A total of 34% of African Americans reported medication trade-offs compared to 11% of Whites ($P < 0.01$). A total of 44% of patients reporting medication trade-offs had median household income of <$20 000 compared to 15% with no trade-offs ($P < 0.001$). Similarly, 88% of patients with medication trade-offs were unemployed compared to 59% unemployed with no trade-offs ($P < 0.001$). More than twice as many patients with limited literacy (65% vs. 32%) reported medication trade-offs compared to those with no trade-offs ($P < 0.001$). No differences were noted with respect to the prevalence of cognitive impairment, organ transplanted (kidney versus liver), or study site. Participants with trade-offs reported lower social support, but this difference did not reach statistical significance.

In univariable results, patients with medication trade-offs were more likely to have ≥3 chronic conditions and were taking more medications (median = 12, IQR: 8,14 with trade-offs versus median= 10, IQR: 7,13 without trade-offs). Most patients received medications from drug stores or mail order pharmacies. The majority of patients (69%) reported private insurance; patients with Medicare were more likely to report medication trade-offs. The median total monthly copays were reported at $40 (IQR: 5,81), 40% of patients reported copays of >$50 per month; there was no association between drug copays and medications trade-offs.

The mean self-reported medication adherence score for the entire medical regimen (the proportion of adherent medications divided by the total number of medications), including chronic disease medications, was 87% (SD = 19); adherence scores were significantly lower among patients reporting medication trade-offs [mean = 77% (SD = 23) with trade-offs versus mean = 89% (SD = 17) without trade-offs, $P < 0.001$]. The mean chronic disease medication adherence score was 77% (SD = 25) among those reporting trade-offs versus mean = 88% (SD = 21) with no trade-offs. No significant difference was noted in transplant medication adherence between the two groups.

A total of 90 (45%) of patients had at least one hospital admission within 12 months after the study interview; there were a total of 160 admissions; 43 admissions among patients with trade-offs and 116 admissions for patients without trade-offs (Table 1). Patients reporting medication trade-offs were more likely to have a hospital admission (61% with trade-offs vs. 42% without trade-offs, $P = 0.05$). A total of 16% of patients had a biopsy-proven rejection episode and 38% had an infection; no differences were noted in these two outcomes when stratified by the presence of medication trade-offs. The reasons for hospital admission are shown in Fig. 1, separately for patients with and without medication trade-offs. The most common admission reasons were infectious or related to postsurgical complications. No significant differences were noted in the reasons for admission among patients with and without medication trade-offs. During the follow-up period, no patients experienced graft loss; one patient died due to recurrent hepatocellular carcinoma at 14 months post-transplant and 11 months following the study interview.

Table 2 provides detailed information with regard to the different types of medication trade-offs. Overall, 17% of patients reported trade-offs; this was equal among LT and KT recipients. The most common trade-offs were "needing a prescription and being unable to afford it in the past 12 months" (11% overall, 12% kidney in KT, 10% in LT) and "making a choice between buying medication and buying food" (11% overall, 9% in KT, 12% in LT). Figure 2 shows the distribution of medication trade-offs across various time points post-transplant, stratified by organ. The majority (59%) of LT recipients reporting medication trade-offs were within 12 months of transplant. By contrast, one-third of KT recipients reporting medication trade-offs were within 12 months of transplantation and greater than half were more than 3 years post-transplant. Demographics and characteristics stratified by organ are shown in Supplementary Table 3.

Multivariable results

Multivariable risk factors for having medication trade-offs are reported in Table 3. Medicare insurance versus commercial or Medicaid, limited health literacy, and having ≥3 comorbid conditions were independently associated with medication trade-offs. Table 4 shows the

Table 1. Demographics, characteristics, and clinical outcomes of study sample stratified by the presence of medication trade-offs.

Variable	Total (*N* = 201)	No medication trade-offs (*N* = 167)	Medication trade-offs (*N* = 34)	*P*-value
Age, *N* (%)				
18–30	12 (6.0)	11 (6.6)	1 (2.9)	0.02
31–45	29 (14)	22 (13)	7 (21)	
46–64	109 (54)	85 (51)	24 (71)	
65–90	51 (25)	49 (29)	2 (5.9)	
Female, *N* (%)	76 (38)	61 (37)	15 (44)	0.41
Race, *N* (%)				
White	137 (69)	122 (74)	15 (44)	<0.01
African American	47 (24)	31 (19)	16 (47)	
Other	16 (8.0)	13 (7.8)	3 (8.8)	
Education, *N* (%)				
High school or less	48 (24)	37 (22)	11 (32)	0.03
Some college	71 (35)	55 (33)	16 (47)	
College graduate	82 (41)	75 (45)	7 (21)	
Annual income, *N* (%)				
<$20 000	39 (20)	24 (15)	15 (44)	<0.001
$20 000–$50 000	50 (26)	39 (25)	11 (32)	
>$50 000	103 (54)	95 (60)	8 (24)	
Employment, *N* (%)				
Full time	43 (21)	41 (25)	2 (5.9)	<0.01
Part time	25 (12)	23 (14)	2 (5.9)	
Unemployed	128 (64)	98 (59)	30 (88)	
Did not answer	5 (3.0)	5 (2.5)	0 (0.0)	
Organ, *N* (%)				
Liver	103 (51)	86 (51)	17 (50)	
Kidney	98 (49)	81 (49)	17 (50)	0.87
Months since transplant, *N* (%)				
<12	68 (34)	53 (32)	15 (44)	0.56
13–24	26 (13)	22 (13)	4 (12)	
25–36	20 (10)	17 (10)	3 (8.8)	
>36	87 (43)	75 (45)	12 (35)	
Limited literacy*, *N* (%)	74 (37)	52 (32)	22 (65)	<0.001
Mild cognitive impairment†, *N* (%)	23 (12)	21 (13)	2 (5.9)	0.48
Low social support‡, *N* (%)	19 (9.6)	13 (7.9)	6 (18)	0.08
Study site, *N* (%)				
Chicago, IL	146 (73)	121 (73)	25 (74)	0.89
Atlanta, GA	55 (27)	46 (28)	9 (27)	
# Of medications, median (IQR)	10 (7,13)	10 (7,13)	12 (8,14)	0.03
Pharmacy type, *N* (%)				
Drug store	100 (50)	78 (47)	22 (65)	0.38
Mail order	58 (29)	52 (31)	6 (18)	
Grocery store	19 (9.5)	16 (9.6)	3 (8.8)	
Discount retail store	5 (3.0)	0 (0.0)	5 (2.5)	
Other	19 (9.5)	16 (9.6)	3 (8.8)	
Medical insurance, *N* (%)				
Private insurance	136 (69)	119 (72)	17 (51)	<0.01
Medicare	40 (20)	26 (16)	14 (42)	
Medicaid	7 (3.5)	5 (3.0)	2 (6.1)	
Self-Pay	3 (1.5)	3 (1.8)	0 (0.0)	
Other	18 (9.0)	17 (10)	1 (2.9)	
Monthly copay, $ median (IQR)	40 (5, 81)	40 (5, 81)	39 (3, 80)	0.98
Monthly copay ≥ $50, *N* (%)	81 (40)	67 (40)	14 (41)	0.91

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Table 1. Continued.

Variable	Total (*N* = 201)	No medication trade-offs (*N* = 167)	Medication trade-offs (*N* = 34)	*P*-value
Medication adherence§, mean % (SD)				
All medications	87 (19)	89 (17)	77 (23)	<0.001
Immunosuppression	93 (20)	94 (19)	89 (25)	0.25
Chronic disease	86 (22)	88 (21)	77 (25)	<0.01
Clinical outcomes, *N* (%)				
Hospital admissions	90 (45)	70 (42)	20 (61)	0.05
Graft rejection	32 (16)	24 (14)	8 (24)	0.18
Infection	77 (38)	63 (38)	14 (41)	0.71

*Cognitive impairment = score of <24 on the Mini-Mental State Examination.

†Limited literacy = score of <4 on the Newest Vital Sign literacy assessment.

‡Low social support = score of <12 on the Lubben Social Network scale.

§Score of 100% = perfect adherence to all medications.

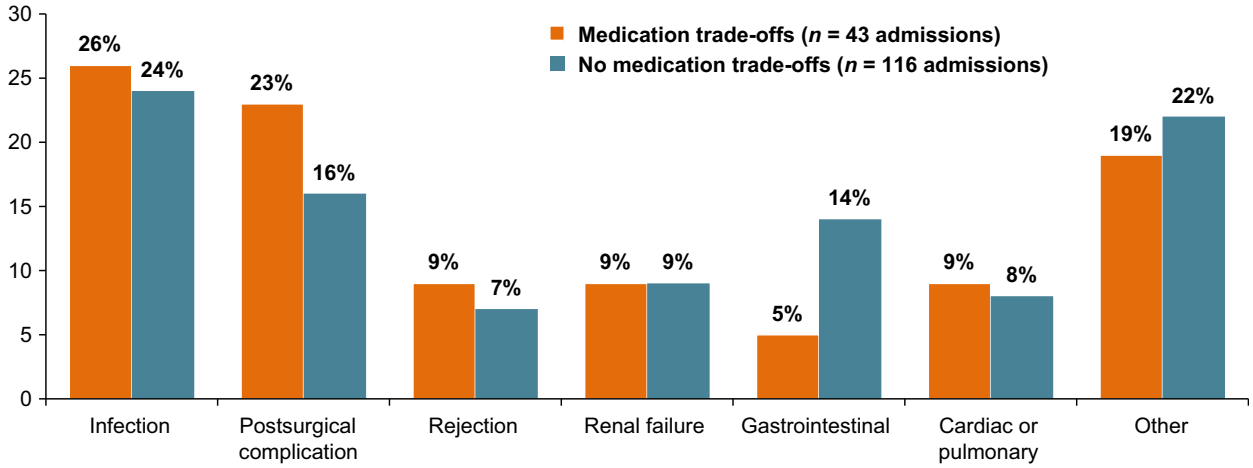

Figure 1 Primary reasons for post-transplant hospital admissions among kidney and liver transplanted recipients. *Y* axis shows the percentage of total post-transplant hospital admissions stratified by reason for admission and the presence of medication trade-offs.

Table 2. Prevalence of medication trade-offs among kidney and liver transplanted recipients stratified by organ.

Type of trade-off, *N* (%)	Total (*N* = 201)	Kidney (*N* = 98)	Liver (*N* = 103)
Needed Rx but could not afford in the past 12 months	21 (11)	10 (12)	11 (10)
Put off paying for Rx to buy food	14 (7)	5 (5)	9 (9)
Spaced out Rx frequency due to cost	17 (9)	6 (6)	11 (11)
Had to make choice between buying Rx and buying food	21 (11)	9 (9)	12 (12)
Presence of any trade-off	34 (17)	17 (17)	17 (17)

Rx = prescription.

multivariable model for the outcome of post-transplant hospital admissions. Post-transplant infections, medication trade-offs, and receipt of LT versus KT were independently associated with post-transplant hospital admission within 12 months of the study interview. Compared to the reference value of no trade-offs, the relative risk (RR) of post-transplant hospital admissions with at least one trade-off was 1.63 (95% CI: 1.03–2.60)

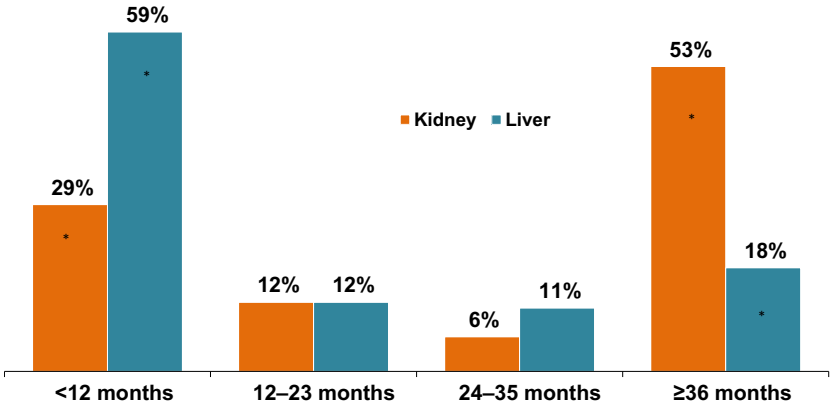

Figure 2 Distribution of kidney and liver transplanted recipients with medication trade-offs across various time points post transplant. *Y* axis shows the percentage of patients with medication trade-offs across each post-transplant time period; *$P < 0.01$.

Table 3. Transplant recipient characteristics associated with medication trade-offs in multivariable modified Poisson regression ($N = 201$).

Variable	RR	95% CI	*P*-value
Non-white race	1.45	0.75–2.80	0.28
Annual income <$20 000	1.33	0.57–3.08	0.51
Transplant within 24 months	1.12	0.53–2.39	0.76
Medicare insurance	2.97	1.19–7.40	0.02
Limited health literacy	2.64	1.23–5.64	0.01
Liver versus kidney transplant	1.50	0.69–3.28	0.31
≥3 comorbid conditions	2.48	1.09–5.62	0.03
# Of medications*	1.08	1.00–1.18	0.04

RR, relative risk.

*For each additional medication.

Table 4. Medication trade-offs and the outcome of hospital admission during 12 months of follow-up: multivariable analysis.

Variable	RR	95% CI	*P*-value
Post-transplant infection	2.37	1.68–3.35	<0.001
Medication trade-offs			
Reference (no trade-offs)	–	–	–
At least one trade-off	1.63	1.03–2.60	0.04
Two or more trade-offs	1.84	1.12–3.02	0.02
Liver versus kidney transplant	1.56	1.10–2.21	0.01

RR, relative risk.

and was 1.84 with two or more trade-offs (95% CI: 1.12–3.02).

Discussion

In a diverse sample of liver and kidney transplanted recipients, we found that about one in eight patients reported medication trade-offs, defined as the inability to afford medications, spacing out medication frequency, or choosing between buying medications and food. Trade-offs were more common within the first post-transplant year among LT recipients, while they were more common ≥3 years after transplant among KT recipients. Medicare insurance, limited literacy, and a higher number of chronic conditions were independently associated with a higher risk of medication trade-offs. Trade-offs were strongly associated with self-reported medication nonadherence and a higher likelihood of post-transplant hospital admissions. Furthermore, the risk of hospital admission was even higher for patients reporting two or more trade-offs. These findings that are consistent with studies focused on populations with chronic diseases [4,25].

Socio-demographic factors largely determined the risk for having medication trade-offs; notably among the patients with medication trade-offs, 65% had limited literacy and 88% were unemployed. Although 34% of African American patients reported medication trade-offs compared to only 11% of Whites, in multivariable analyses the association between race and trade-offs was attenuated as the racial differences were explained by disproportionately higher rates of poverty and limited literacy among African Americans. The finding that Medicare insurance was associated with greater trade-offs was initially surprising; however, conceivably, patients with primary Medicare insurance did not have supplementary coverage for outpatient visits and transplant immunosuppression (Part B) and prescription drug coverage for other medications (Part D). This finding would need to be prospectively verified.

Importantly, limited literacy was found to be an independent risk factor for medication trade-offs in this study. A sizable body of evidence in the general chronic disease population has shown that limited heath literacy (defined as the ability to comprehend and use health information to make health decisions) is associated with increased hospitalizations and death [26–28]. Recent studies by this group showed that limited literacy was an independent risk factor for poor medication knowledge among LT and KT recipients, resulting in increased post-transplant hospital admissions [29,30]. In the context of medication trade-offs, a limited capacity to understand and use health information (e.g., understanding the importance of taking medications) may impact a patient's financial choices regarding whether or not to skip essential medications.

Although no differences in medication trade-offs were reported by organ type, the answers on the trade-offs questionnaire differed depending on the time from transplantation. Most LT recipients reporting trade-offs were within 12 months of transplantation, during a time when they were presumably taking the most medications. By contrast, most of the KT recipients reporting trade-offs were ≥3 years from transplantation. The possible explanation for these differences is that Medicare ceases to provide prescription coverage to KT recipients after 3 years from transplantation whereas LT recipients are generally required to maintain prescription coverage in order to be eligible for transplantation [16].

Notably, patients reporting medication trade-offs had lower self-reported adherence for chronic disease medications, but not for immunosuppression drugs. It is likely that patients with financial difficulties may have been prioritizing transplant immunosuppression over chronic disease medications. Studies have long shown that transplanted recipients have a higher prevalence of hypertension and diabetes than the general population [31] placing them at higher risk of end-stage renal disease and cardiovascular complications, and highlighting the importance of promoting long-term adherence to chronic disease medications [32,33]. An important question is how to address financial barriers to long-term chronic disease management in this patient population. Improving adherence by providing expanded prescription coverage for patients with chronic conditions has been explored in clinical trials and theoretical models. Recent data by Choudhry *et al.* [34] showed that providing full prescription coverage for cardiac medications after a myocardial infarction resulted in improvements in medication adherence and reduced rates of vascular events. Yen *et al.* [35] found that extending Medicare prescription coverage for life in KT recipients would still be cost effective even if used by <91% of recipients. However, patient self-management behavior is complex and is not solely driven by financial factors, as also shown by Chisholm *et al.* [36], who reported on decreased medication adherence 12 months after transplantation even when free immunosuppression was universally provided.

Despite strict psychosocial selection criteria and the general requirement for insurance coverage prior to listing a patient for an organ, it must be acknowledged that financial barriers play a role in post-transplant nonadherence and influence post-transplant outcomes. In addition, a recipient's financial situation may change over time and there may be stigma in acknowledging the inability to afford post-transplant medications. The introduction of immunosuppression for transplantation may paradoxically lead to worse chronic disease self-management over the long term if patients are skipping essential nontransplant medications. Therefore, brief assessments of patients' ability to afford medications at annual post-transplant appointments may provide important insights into their financial situations as well as an indirect measure of adherence. Furthermore, financial barriers in transplanted recipients are often modifiable as transplant centers can assist patients with drug copays and by utilizing generic medications. Studies should evaluate using this screening tool at the transplant evaluation visit as well periodically post-transplant.

There are certain study limitations that must be acknowledged. Interviews were conducted at two racially diverse transplant centers; however, findings may not be generalizable to transplanted recipients elsewhere; furthermore, non-English speakers were excluded in this exploratory pilot study potentially biasing results. Future studies should include patients with limited English proficiency. Insurance information was collected, but no specific data were obtained on medication prescription plans and there was no accounting for annual deductibles. Medication adherence was assessed via self-report and could have been underestimated and we did not measure adherence to medical appointments [37]. We also did not assess how medication side effects may have impacted nonadherence. The cooperation rate was 58% potentially introducing bias. Although medication trade-offs were associated with hospital admissions, it cannot be assessed whether they directly or indirectly causative. In addition, as convenience sampling was used, patients who chose

not to participate may have been more or less likely to experience medication trade-offs potentially biasing the results, although there were no differences in demographics or time since transplantation between patients who enrolled and those who opted out.

In conclusion, medication trade-offs were common among liver and kidney transplanted recipients and present at various time points post-transplant. Medication trade-offs were associated with lower self-reported adherence to chronic disease medications and post-transplant hospital admissions. Brief, routine assessments of financial barriers to proper medication adherence such as the medication trade-offs questionnaire may be warranted in clinical to improve long-term post-transplant outcomes.

Authorship

MS: involved in study design, data collection, data analysis, interpretation of the data, drafting of the manuscript, and final approval of the manuscript. PR: involved in interpretation of the data, critical revision of the manuscript, and final approval of the manuscript. RP: involved in data collection, data analysis, interpretation of the data, critical revision of the manuscript, and final approval of the manuscript. JL and MW: involved in study design, interpretation of the data, critical revision of the manuscript, and final approval of the manuscript.

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Conflict of interest

The authors declare no conflict of interests.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Baseline demographics and characteristics of patients prior to study recruitment.

Table S2. Univariable associations of patient demographics and characteristics with post transplant hospital admissions.

Table S3. Demographics, characteristics, and clinical outcomes of study sample stratified by organ.

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