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Medication-taking among adult renal transplant recipients: barriers and strategies

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Summary

Medication adherence is essential for the survival of kidney grafts, however, the complexity of the medication-taking regimen makes adherence difficult. Little is known about barriers to medication-taking and strategies to foster medication-taking. This cross-sectional study involved semi-structured interviews with 82 kidney transplant recipients approximately 2 months post-transplant on medication-related adherence, barriers to medication-taking, and strategies to foster medication-taking. Although self-reported adherence was high (88%), qualitative analysis revealed that half of the patients (49%) reported experiencing at least one barrier to medication-taking. The most common barriers were: not remembering to refill prescriptions (13%), changes to medication prescriptions or dosages (13%), being busy (10%), forgetting to bring medicines with them (10%), and being away from home (10%). The most common strategies to foster medication-taking were: maintaining a schedule of medication-taking (60%), organizing pills using pillboxes, baggies, cups (42%), bringing medicines with them (34%), organizing pills according to routine times (32%), and relying on other people to remind them (26%). Understanding the range of barriers to adherence and strategies kidney recipients devised to promote medication-taking may help transplant clinicians to better educate transplant recipients about appropriate medication-taking, mitigate the risk of medication nonadherence-related rejection, and may help inform patient-centered interventions to improve medication adherence.

Introduction

Kidney transplantation is the treatment of choice for selected patients with end-stage renal disease (ESRD) [1,2]. Each year, about 17 000 patients receive deceased or living donor transplants [3], and there are currently over 145 000 renal transplant recipients with functioning allografts in the United States [4].

Adherence to taking immunosuppressants is essential for the survival of transplanted kidney grafts. Nonadherence has serious consequences, including infection, rejection episodes, and graft loss with consequent resumption of dialysis [5]. In fact, nonadherence is the one of the leading causes of renal graft loss after patient death with a functioning graft, cellular allograft rejection, and systemic infection [6]. However, despite its vital importance, medication adherence can be difficult to attain and maintain for a variety of reasons.

Kidney recipients must take two to three immunosuppressants once or twice daily, and at consistent times, to ensure sufficient and steady blood drug levels to maximize their anti-rejection effect. Over the weeks and months following transplantation, medications and dosages are often changed to obtain optimal immunosuppression while minimizing side-effects. Kidney recipients also take, on average, eight to 10 transplant-related medications daily [7], as well as prophylactic anti-infective medications, anti-ulcer medications, and medications for comorbidities and risk factors that contribute to ESRD, such as diabetes [8]. Immunosuppressants may cause serious and/or stressful adverse side-effects and conditions, including diarrhea, sleeplessness, weight gain, skin cancer, and greater risk of infection [8], which can hinder adherence [9,10].

Medication nonadherence is common, occurring in 5% to more than 45% of renal transplant recipients [5,11,12], and adherence declines over time [13]. Recent studies report that 19.3% of kidney recipients had not taken their immunosuppressive drugs at least once within the past 4 weeks [14], which is comparable to rates found in lung (13%) and heart (21%) transplant recipients [15]. Given the frequency of nonadherence and its adverse effects on transplant outcomes, understanding barriers to adherence and strategies patients use to enhance adherence is essential for several reasons including: educating kidney recipients about helpful strategies to promote adherence, offering tools to help recipients overcome the barriers to medication-taking, preparing healthcare providers to avoid common pitfalls in prescribing regimens, and devising interventions that promote medication-taking. The purpose of this study is to examine social, structural, and cultural contextual factors that hinder and foster adherence to immunosuppressants among adult kidney transplant recipients.

Background

In this section, we describe theoretical and methodological limitations of prior research on adult kidney transplant recipients' adherence to immunosuppressants in terms of the following characteristics: (i) barriers to medication-taking or reasons for nonadherence, (ii) study design and type of data collected, and (iii) treatment length of time.

Very little research has examined in-depth contextual factors that affect adult kidney recipients' medication-taking practices. Few studies have investigated strategies patients mobilize to ensure appropriate medication-taking [16], or cognitive representations (or perceptions) of transplant medications that might inform their behaviors. The little work done on barriers to adult medication-taking has examined the reasons for or health beliefs related to post-transplant nonadherence [9,10,17–19]. Documented reasons for adult nonadherence include: forgetfulness, cost, unpleasant side-effects, regimen complexity, and low palatability [10,19,20]. Among pediatric patients, reasons for nonadherence include reasons similar to adults, e.g., poor medication taste, but also focus on issues of responsibility for medication-taking, body image, and troubled adolescence [21–23], which limits comparison to adults. Further, studies consistently show that stronger beliefs in the importance of immunosuppression are positively related to adherence [9,16,24–26]. One survey of 1,402 kidney recipients categorized nonadherent patients as 'accidental noncompliers' (47%), 'invulnerables' (28%), and 'decisive noncompliers' (25%) based on their beliefs about immunosuppression [18,25]. Whereas accidental noncompliers sometimes forgot to take their medication, invulnerables believed they did not need to take their medications regularly, and the decisive noncompliers made decisions independent of their health care provider about whether or how to be adherent with their medication regimens [18,25]. That most patients were 'accidental noncompliers' suggests that factors beyond the patient's control, e.g., social, cultural, structural factors, frequently affect medication-taking. Barriers to adherence are as multifactorial for patients with other chronic illnesses as they are for kidney recipients. Notably, attitudinal factors contributing to intentional nonadherence included health beliefs, complex medication regimens, lack of routines, not being convinced of the need for all their medications [27] and treatment of asymptomatic conditions [28]; while structural factors contributing to unintentional nonadherence included difficulties with maintaining continuity of care with care providers [27].

Methodologically, most research on adherence in kidney recipients uses a retrospective design and quantitative approaches. Little work has used qualitative or combined qualitative with quantitative approaches, e.g., [16], which are valuable because they can elicit previously unidentified barriers, and provide an in-depth understanding of factors contributing to nonadherence over time from a patient's perspective [29]. Russell *et al.* [16] interviewed 16 patients with a transplant for 0 to over 24 months, and found that, for example, experiencing disapproval from loved ones about taking medications served as a barrier to medication-taking. Conversely they found that patients devised systems to foster medication-taking, including planning ahead and organizing, using a pillbox, keeping extra medications on hand, receiving reminders from others, and using a clock and cues for remembering, among others [16].

Another study design limitation of prior studies pertains to the issue of treatment length of time. Most research has predominantly focused on patients who have had their transplant for a year or more, as Russell *et al.*

[30] point out. However, this early period may be formative in establishing self-care habits.

This paper reports new kidney transplant recipients' rates of self-reported adherence, their levels of self-efficacy for medication-taking, and barriers to and strategies for remembering medication-taking. By 'barriers,' we refer to 'negative resources found to be associated with poor health outcomes by interfering with one or more aspects of the self-care management process' [31:396]. By 'strategy,' we refer to ''actions taken to mobilize resources and maximize favourable outcomes' [32:462, 33:525]. We also examine the social (interpersonal) and structural (e.g., access to care, organization of work time) contextual factors that shape how kidney transplant recipients make taking medications fit into their daily routines using both quantitative and qualitative methods.

Conceptual model

Our study is guided by Leventhal *et al.*'s [34] self-regulation model of illness management. This model derives from social cognitive theory, which is based on the idea that people learn strategies to manage their chronic illness through the self-regulation processes of observations, judgments, and reactions [35]. That is, people observe their own medication-adherence behavior, judge whether the behavior was successful in achieving their goal, and react to the experience [35–37]. Kidney recipients' self-regulation processes are also expected to be based on feelings of self-efficacy and their health beliefs. Self-efficacy is the assessment that one can effectively perform a behavior to achieve a desired goal or outcome [35]. High self-efficacy for medication-taking is expected to be guided, in part, by internal resourcefulness, health status, or the absence of barriers and/or the availability of strategies for fostering adherence. Low self-efficacy for taking medications has been shown to be a predictor of medication nonadherence among kidney transplant recipients [7,38], and identified as a pathway by which nonadherence contributes to late acute kidney rejection [39].

Methods

Study population

All adult kidney transplant recipients were recruited in an incidence cohort from Loyola University Medical Center (LUMC) in Maywood, IL (July 2004–May 2006) and Albany Medical Center (AMC) in Albany, NY (September 2006–November 2007). Kidney recipients were eligible for participation if they: were aged 18 years or more, spoke English, and received a kidney transplant within the previous 6 weeks. Patients were recruited early post-transplant in order to prospectively examine the social and cultural factors and experiences that may affect adherence behavior early on. All eligible patients were approached for participation into the study until the end of data collection. We approached eligible patients in the transplant clinic waiting room and described the study to obtain initial oral consent and contact information for those interested in participating. For those who provided oral consent, we arranged a date for the interview or called them later that week to set the date.

Qualitative and qualitative approaches

We used a combination of qualitative and quantitative methods to: assess levels of adherence, examine patterns of medication-taking barriers and strategies, and compare findings across participants [40]. Using a combination of quantitative and qualitative approaches simultaneously offers many advantages to collecting and analyzing data. While quantitative approaches enable the researcher to establish relationships among the variables, the qualitative components help to explore and explain the reasons for those relationships [29]. Qualitative methods are best suited to describe phenomena in depth by taking into consideration the role of context or intervening variables in shaping a given process or event [41]. Qualitative methods are flexible in that open-ended interviews allow respondents to discuss issues of significance without imposing the researcher's own ideas or a predetermined set of cognitive categories. Thus, the use of qualitative methods is ideal for understanding how respondents think about a given issue from their own point of view.

Interview

Semi-structured interviews were conducted approximately 2 months post-transplant, either in person or by telephone, by one author (EJG) or a research staff member. All interviews were tape-recorded with an average duration of 2 h. Respondents were provided $20 to compensate for their time. The data reported herein are part of a larger, longitudinal study examining self-care (medication-taking, physical activity, fluid intake, diet); the impact of social support, finances, and health beliefs on self-care; and how self-care practices affect kidney graft outcomes. This paper reports results from the first interview. Accordingly, we recruited study participants and collected data beyond the point of saturation to ensure sufficient numbers for statistical analysis. Institutional Review Board approval was obtained from Loyola University Medical Center and Albany Medical Center. Study participants provided written informed consent. The interview questions were initially pilot-tested with four transplant coordinators and two social scientists.

Topics covered in the interview, as they pertain to this paper, included both closed- and open-ended questions about: (i) medication-taking adherence; (ii) strategies patients mobilize to enable medication-taking; (iii) barriers to medication-taking; (iv) demographics; and (v) medical information.

Measures

Adherence was assessed by asking patients whether or not they have, since their transplant: not taken anti-rejection medicine intentionally; been in a situation that prevented them from taking anti-rejection medicines; tried to 'stretch' medications or make medicine last longer by taking a little bit less than prescribed; taken more or less than the required dosage of anti-rejection medications; and taken anti-rejection medicines regularly at the same times in the day. All responses were dichotomous. When applicable, we elicited the reasons for why they intentionally did not take anti-rejection medicine.

Strategies to foster medication-taking were assessed using open-ended questions: 'Do you have any routine or way to remind yourself to take your transplant medicines?' Those who responded 'yes' were asked to describe their strategies. Patients were also asked: 'How do you make taking your pills fit into your daily life?' and 'Tell me about your routine.'

Barriers to medication-taking were assessed using both open-ended and closed-ended questions. Open-ended questions included: 'What are some of the things that make managing or taking your transplant-related medicines difficult?' and 'Why is that difficult for you?' The closed-ended questions asked patients to indicate whether or not any of the following barriers applied to them: 'Not remembering when to refill prescriptions,' 'Changes to medicine prescriptions or dosages,' 'Not having enough money to buy medicines,' 'Not remembering when to take medicines,' 'Not getting access to the pharmacy to pick up medicines,' and 'Not remembering how much medicine to take.' Response options included: 'applies' or 'does not apply.'

Demographics included age, gender, race/ethnicity (which was based on self-identification), marital status, education, employment status, income, and primary insurer.

Medical information included cause of ESRD, organ donor source, number of transplants (dichotomized as one or more than one), and time with a transplant as of the date of the interview. This information was obtained from patient self-report and confirmed through medical record review.

Self-efficacy for medication-taking was assessed using the Long-Term Medication Behavior Self-Efficacy Scale [42]. The 27-item instrument rates long-term medication-taking on a five-point Likert scale anchored by 'very little' and 'quite a lot.' A higher score indicates a higher level of perceived self-efficacy. Cronbach's α has been reported as 0.86 [7].

Health status, a measure of overall self-rated health, was assessed with a single global item, 'How would you rate your health compared with people your age with a transplant?' ('excellent,' 'very good,' 'good,' 'fair,' and 'poor').

Data analyses

Statistical analysis

Descriptive statistics were used to summarize the demographic, clinical and psychosocial predictors of medication adherence and self-efficacy for medication-taking. For the simple analysis of medication adherence, associations with categorical predictors were tested using Pearson's Chi-squared test, while *t*-tests were used for associations with continuous predictors. Two-sample *t*-tests were computed for dichotomous predictors and one-way analysis of variance was used for trichotomous predictors of self-efficacy. Spearman correlation coefficients and associated *P*-values were calculated for continuous predictors of self-efficacy. Respondents who did not answer a question were excluded from analyses. All tests were two-tailed and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS 15.0 (SPSS, Inc., Chicago, IL, USA).

Content analysis

The tape-recorded interviews were transcribed verbatim [43]. Open-ended responses were analyzed by content analysis using The Ethnograph 15.0 [44]. This entails the systematic search for themes and repetitions emergent from the data [45,46]. An initial set of participants' barriers to and strategies for medication-taking were coded and a preliminary coding scheme was developed. The codes were applied to a new group of patient responses, the coding scheme was revised to adjust for new responses, and modified codes were applied to the previous set of responses. We continued in this manner until no new codes emerged and saturation was achieved [45]. Codes were generated from topics identified in advance (e.g., 'barriers to medication-taking') [47], and from the data. One author (EJG) and a research staff member separately coded interviews, then compared and resolved discrepancies in codes to establish inter-rater reliability as 93.7% [48]. The frequencies of responses to each theme are included to highlight the magnitude and commonality of the themes.

Results

Demographics

Of 143 eligible patients, 82 participated in an interview, for a 57.3% response rate. Twenty-four percent (*n* = 35) refused to participate because of slow recovery from the operation (feeling overwhelmed with the transplant), time commitments (e.g., returning to work, extensive time investment by participating in the study), burden of paperwork involved, or disinterest, and 18% (*n* = 26) gave oral consent but have not yet provided written consent and/or were unable to be reached for an interview. Table 1 presents the demographic characteristics of the sample, which generally reflect the average age and gender profile of ESRD and kidney transplant recipients nationally [49].

Medication-taking practices

We found high rates of self-reported adherence (88%) (see Table 2). That is, for 12%, situational factors or unforeseen circumstances prevented patients from appropriately taking their immunosuppressant medications. Only one respondent reported not taking medications on purpose. Few (8.5%) reported inconsistency in the timing of taking their medications. Some (5%) patients reported altering the dosages of their medications. No differences in adherence were found between the two transplant centers represented.

Twelve percent reported having been in a situation that prevented them from taking their medications. The following quote illustrates such a situation:

> Once, I took some medication maybe like, 4 h later than I should have. And that's just because I was at a Sox game last Sunday and that went into extra innings.…I didn't get home 'til like, 1:30 in the morning, and I had to take some of the medication at 9:00.…Sometimes I stretch it until like, 10:00, 10:30 or whatever, which normally I'm already back home by that time. And, not this time. (#10056).

Self-efficacy for medication-taking

Overall, patients' self-efficacy with taking medications was relatively high, with an average score of 4.6 (SD: 0.542) (range: 2.0–5.0). Self-efficacy was not associated with demographics or adherence.

Barriers to taking anti-rejection medicines

Patients reported different types of barriers to medication-taking depending on how the question about it was asked. Among the quantitative questions, barriers to taking anti-rejection medicines endorsed by kidney recipients

Table 1. Demographic, medical, and psychosocial characteristics of study participants (*N* = 82).

Variable	*N*	%
Demographics		
Age (years), mean (SD) (range)	47.3 (12.3) (18–74)	
18–48	44	53.7
49–74	38	46.3
Gender		
Female	35	42.7
Male	47	57.3
Ethnicity/race		
White	56	68.3
African American	15	18.3
Hispanic/other	11	13.4
Marital status		
Married	52	63.4
Not married	30	36.6
Education (years), mean (SD) (range)*	14 (3.33) 6–27	
≤High school	31	37.8
High school grad/GED	50	61.0
Employment status*		
Employed	41	50.6
Unemployed/student	39	48.1
Gross household income*		
<\$14 999–\$29 999	21	25.6
\$30 000–\$59 999	22	26.8
\$60 000+	32	13.4
Primary insurer*		
Private insurance	42	51.9
Medicare/Medicaid	39	48.1
Health status		
Cause of ESRD		
Diabetes	7	8.5
Hypertension	20	24.4
Glomerulonephritis	18	22
Other	37	45.1
Organ donor source		
Deceased donor	46	56.1
Living donor	36	43.9
No. transplants		
1	65	79.3
2+	17	20.7
Time with a transplant (months), mean (SD) (range)	1.58 (0.963) (0.5–6.5)	
Self-rated health		
Excellent	13	16
Very good	30	37
Good	28	34.6
Fair	9	11.1
Poor	1	1.2
Self-efficacy, mean (SD) (range)	4.69 (0.495) (2.0–5.0)	

ESRD, end-stage renal disease.
*Total *n* does not add up to 82 because participant(s) did not know or disclose information.

Table 2. Nonadherence to anti-rejection medicines*.

Types of nonadherence	Rates of nonadherence *N*	%
Not taken medications as prescribed	10	12.2
Intentionally not taken medicines	1	1.2
Stretched medicine	3	3.7
Changed the dosage of medicine	4	4.9
Not consistent with time of medication-taking	7	8.5

*Percents do not add up to 100% as participants responded to each item separately.

included: when prescriptions or dosages change (13%); not remembering to refill prescriptions (13%); not having enough money to buy medications (9%); not remembering when to take medicines (9%); not getting access to the pharmacy to pick up medicines (6%); and not remembering how much medicine to take (4%).

The open-ended question about barriers elicited more responses. Half of all patients (49%) reported experiencing at least one barrier, and 16% reported experiencing two or more. These barriers fall into four categories: (i) personal schedules, routines, and health; (ii) characteristics of medicines; (iii) medication dosage and scheduling; and (iv) access to medicines and pharmacies.

Personal schedules, routines, and health

Barriers pertaining to patients' personal schedules and health included: being busy, forgetting to bring medications when away from home, unanticipated events occurring when away from home without medicines, sleeping late, feeling sick, and side-effects.

Patients ($n = 8$) reported *being busy* as being caught up in an activity that distracted them from remembering their medications. As the following statement reveals, being busy minimized receptivity to cues to take medications, even when at home:

> The other day, I didn't take my morning medications until later, because I totally, 'cause I got into work mode, I got home and I'm like, I have to do this, this and this. I totally, totally forgot to take them until it was almost after 3:15. I know that was horrible… (24-year-old white female #12322)

Eight other patients reported *forgetting to bring medications with them* when leaving their house. As one patient stated:

> When I leave the house, remembering to put them in a baggie. Sometimes I just leave the house, and then I just like, I have to run back in…That's probably the most difficult. (32-year-old Hispanic male #10056)

Other patients ($n = 8$) also reported *being away from home* made them more likely to forget to take their medications. They are less aware of the time when away from home, likely because they do not have routine cues available. Patients expressed concern that unanticipated circumstances, such as being out to dinner or at a ball game later than expected, may prevent them from accessing or remembering their medicines.

> But, sometimes when you are out you are not as conscious of the time as you are at home. So, it is like 8:15, you think, 'Oh, I didn't even know what time it was.' But, you know, I think, I don't know if I can live like that. (51-year-old white female #10009)

Few patients ($n = 4$) stated that *sleeping later* on the weekends interfered with staying on their medication schedule, as one patient noted:

> Sometimes you wake up late. Usually, it's the morning one. You wake up later and, like I said, you want to eat something before you take them. (28-year-old white female #10031)

Four patients reported that *being sick* made taking medications difficult because keeping the medications in their stomach can be a problem. One patient helped her body accept the medications by taking them in a certain order:

> I don't think it's difficult unless you're sick or you're nauseous or something then it could be difficult, but other than that I don't think it's difficult to take medicine. [Interviewer: Say, for example, you are sick or nauseous, how do you take them then?] Well, first I would take the Zantac first to, you know, help settle my stomach, but then if it still doesn't go down or if you throw them up then I'd have to come here and you'd have to get them by IV if you can't keep them down. (28-year-old white female #10031)

Other patients ($n = 5$) reported how side-effects from the medications interfered with medication-taking, as the following illustrates:

> But, at first, your hand shakes from the Cyclosporine, your stomach hurts from the medicines, you know, Prednisone makes your face puffy, you know, you win some, you lose some, but, what are you going to do. (51-year-old white female #10009)

Medicine characteristics

Patients expressed concerns about the characteristics of medicines that made ingesting them difficult. Specifically, patients reported disliking their *large size* ($n = 5$), *bad taste and smell* ($n = 6$), and the *large quantity* of medicines required ($n = 2$). For example:

> ...the bigness of the pills. They are huge, and all the pills that I got–I can't swallow them all at one time.

> I have to sit there and just get a few down at a time, y'know. That's nerve wracking–trying to take all of them.…My wife told me today, 'You want me to crush them in applesauce? <laughs> (45-year-old African American male #10051)

Medication dosage and scheduling

Unlike the unfavorable qualities of medicines noted in the barrier above, concerns about medication dosage and scheduling pertain to how patients must take the medicines. Two participants reported that the *timing of their dosing schedule* made taking medications difficult in two ways. First, dosages to be taken every other day were perceived as too infrequent to remember. Second, dosages prescribed to be taken 1–2 h after taking other medications were also difficult to remember. One patient explained how taking liquid medicines was more difficult than pills because of the timing involved:

> I mean, at first, it was difficult…in the sense that I was, for the first week or 10 days I was overwhelmed with you know, these all new medicines and that some of them could not be taken within 2 h of an anti-acid or iron... (41-year-old Hispanic male #12318)

A few patients ($n = 4$) experienced difficulty when their *prescriptions or dosages changed*. As one patient explained, the original instructions on the medication bottle label confused her when the dosage changed:

> I notice that- Yeah, because I can get caught up in a routine and then they switch it up and I'm like, Oh, my God. You know. And my mind is still set- especially if the bottle- see like now, this one I was taking four, so I had to write that on there. Had to write three. You know, whereas if I didn't write that on there, I'd still be taking four, you know. So…if they change it. (36-year-old African American female, #10028)

Another patient expressed concern about the complexity of the various medication dosages:

> Well, knowing what pills, you know, you got a lot of different pills–knowing which ones–making sure you got the right ones. That complicates it too, you know, making sure you got the right medicine in the cup and you're not overdoing it or underdoing it. That can get complicated. (45-year-old African American male #10051)

Access to medicines and pharmacies

It is common for patients to order a 3-month supply of immunosuppressants through an on-line pharmacy. Because certain medications require refrigeration, it is essential for patients to coordinate the timing of delivery with their personal schedule. Accordingly, some ($n = 7$) patients identified problems relating to the *process of ordering refills* from the pharmacy, *remembering* to order refills, and coordinating the *timing of delivery*. For example, one patient described her experience:

> So, yes, I am having a difficult time remembering to call them or send in a prescription and when is it gonna be delivered and making sure I'm home, so it's taking me a little time to do this. (41-year-old white female #10039)

This example illuminates well how patients experience difficulty with coordinating the timing and scheduling of different medicines, which may undermine efforts to establish and maintain routines that are critical to appropriately taking medicines. The manner in which patients develop medication-taking routines will be discussed below.

Strategies to aid in remembering

Respondents reported five key strategies that help them remember to take their medications: (i) establishing systems of visual cues; (ii) relying on external aids; (iii) relying on internal resources; (iv) organizing medicines; and (v) toting medicines.

Establishing systems of visual cues

Patients used several systems that helped them remember to take their medicines, and had to actively engage or interact with these systems in order for them to be effective. A fifth of the patients ($n = 17$) kept medications visible by storing them in the open, especially in their kitchen, as the following statement illustrates:

> I keep that out on my counter, so you know, when I walk, so it really gives me an idea of, I can look at it and say: 'Did I take my morning meds? Oh yeah, they're gone. Oh no, I didn't take them.' So I can look at them. (36-year-old Native American male #12321)

Some patients ($n = 15$) used a chart or list of medicines to refer to as they prepared to take their medications, as the following shows:

> …go in and I do it myself, I know I'm doing it right, I have the chart right in front of my meds, I have them all in a row of how I take them, so that they're all lined up in the order that they're on the sheet. And that's how I do it. (51-year-old white male #12324)

Eleven patients reported updating their medication chart after receiving notification of medication changes. Lastly, a few ($n = 4$) patients stated that they ensured having access to clocks around them so that they could pay attention to the time for proper medication-taking.

Relying on external aids

Over a quarter of patients relied on external aids to actively remind them to take medications, including other people ($n = 21$), and technological devices such as clocks, watches, PDAs, and phone alarms ($n = 14$). Patients relied on family and friends to remind them, with a few patients intentionally telling others to remind them at times of the day or teaching others the medication regimen as a backup in case the patient forgets. For example:

> But at nighttime if I lay down after dinner, my son– when he's here, I always tell him, 'You know, make sure I'm up at 8 to take my meds.' Which, he does. Even if I'm awake watching TV, he comes out to make sure. (49-year-old white female #12297)

Relying on internal resources

The third strategy entails patient-driven efforts to help them take medicines. For over half the patients ($n = 49$), being on a schedule helped fit medicines into their daily routines, as the following illustrates:

> No, I just take them when I'm supposed to.…I know when I first get up there's pills I gotta take and then I don't take the rest of my pills until after I get my blood drawn in the morning. And then I take the rest right at dinnertime. So it's basically– I'm on a schedule, so. (35-year-old white male #12301)

Other patients ($n = 17$) reported remembering to take their medicines on their own without using any aids, as the following statement shows:

> I basically remember. I don't have any aids to remind me to take my medication. I know that I have to take them at this and this time and nobody reminds me. I don't have an alarm or anything like that. (53-year-old white male #10027)

A subgroup of patients ($n = 6$) reported wanting to control their lives, show responsibility for their health, and recognized that appropriately taking medications was a way to prioritize their health.

Organizing medicines

A fourth strategy consisted of organizing medicines. While most patients organize their medicines in some fashion, these patients did so explicitly to help them remember to take the medicines. Many patients ($n = 34$) organized their pills using devices such as pill boxes.

> I got a pill box that says, 'morning,' 'night.' <laughs> [EG: Is that working out for you?] Yeah, that works out really well. If I got an empty slot, I know I took them. If they're in there, it's like, 'Oh, okay.' It's become a routine... (41-year-old white male #12282)

Establishing routine times to organize their medications also fostered medication-taking ($n = 26$). Most of these patients typically organized their pills once a week or every couple days. Few patients ($n = 3$) reported that their spouse set up medicines. Having a routine way to organize pills helped patients to ensure an adequate supply and remember which medications must be taken, as the following shows:

> I do like a three check which I was taught when I used work for the state.…There's a three-check system before giving out meds, you have to refer to, which I do at home, and it's just a little bit different system....When I set my pills up, I go by my med paper that they gave me in the hospital, breakfast, lunch and dinner, and all that. And I set it up for the whole week and I check that, and then I have it on my calendar also, I check. And I go through my pills and I check my bottles after I have them in my box, I can see through the box and I refer back to the bottles also to make sure that I have the right pills, the right dose….. (46-year-old white female #12313)

Some patients ($n = 9$) reported that they use mail order to help them remember to refill their medications.

Toting medicines

A third of patients ($n = 28$) reported bringing either a day's worth of medicines or all of their medicines with them wherever they went or when going out of the house, as illustrated by the following:

> I carry with me 2 weeks' worth just in case, God forbid, anything happens and I can't get home to it, you know....If I go somewhere long distance, you know, so. It's necessary for my life. (46-year-old African American male #10037)

Medication-taking becomes automatic

As a result of implementing these strategies, a third of patients ($n = 25$) reported that taking medications has become a 'habit' or 'automatic' to them. Patients expressed just how ingrained the process of medication-taking has already become to them through several revealing phrases, including: 'natural,' 'second nature,' 'mechanical,' 'conditioned,' 'standard,' and 'robotic.' The following example conveys how patients are not consciously attentive to medication-taking, but rather the habit has become embodied routine:

> It's just like *it happens naturally* now.…*My body may just look* at my watch, and it might be 7:00 and then I know it's time to get ready because I take it at 8:00; so it's just like an *automatic* thing. (42-year-old African American male #10021, emphasis added)

It is apparent that these patients, at only 2 months post-transplant, have already developed the medication-taking habit.

Discussion

Our study examines, in-depth, new kidney transplant recipients' barriers to medication-taking, and strategies to enhance adherence. We found high rates of self-reported adherence. This finding is likely related to patients being newly post-transplant, still in the honeymoon period and too fearful and/or grateful for the kidney, to not follow treatment requirements. Other studies of self-reported adherence report comparable [50,51] or lower rates of adherence [5,7,52] but most of these studies are typically conducted at least 1 year post-transplant. Despite the high rates of adherence, patients at this early post-transplant stage already face a number of barriers to medication-taking. Given that adherence decreases over time [13], these data represent a useful baseline from which to compare future adherence patterns. Additionally, our findings may better enable clinicians to predict renal transplant patients who are most likely to be nonadherent to their immunosuppressant therapy.

Leading barriers to medication-taking were not remembering to refill prescriptions and changes to medication prescriptions or dosages, consistent with other studies [53,54]. Our qualitative inquiry revealed additional barriers that have not been previously identified, including being busy, forgetting to bring medicines with them, being sick, and being away from home. We also found that an important social factor affecting access to medications was the difficulty patients experienced in the process of ordering refills from pharmacies for a timely arrival and coordinating their timely delivery. As many patients reported more than one barrier; it is likely that the greater number of barriers increasingly exacerbates patients' efforts to appropriately take medicines. Research on adolescent kidney recipient medication-taking found that those with a higher perceived number of barriers missed significantly more doses ($P < 0.004$) and were more likely to be late taking medications ($P < 0.001$) [21], suggesting the need to reduce the barriers that the patients perceive as being encountered.

The most common strategies patients used to adhere to their medication regimen were: maintaining a schedule of medication-taking, organizing pills, carrying medicines, organizing pills according to routine times, and relying on reminders from others. Other research has similarly documented how organizing medications, using pill boxes, and receiving reminders from others facilitate adherence [16,38]. Russell *et al.* [16] similarly found that patients relied on visual cues and external aids, such as clocks; our qualitative findings revealed a broader array of cues that patients used including maintaining medicines in open view and relying on technological devices.

Identifying strategies patients use to foster medication-taking is important for educating and preparing transplant candidates and recipients. Investigating medication-taking barriers of transplant candidates may reveal helpful strategies for improving adherence post-transplant, as has been examined in pediatric candidates [21]. A study of transplant coordinators found that they recommended various strategies to enhance medication-taking, including using pill boxes and alarms to foster medication-taking [55]. It may be helpful for transplant centers to provide kidney recipients and their families with kits containing pill boxes, monthly schedules, timers, and information on where to purchase watches with multiple alarm capacity. Moreover, pharmaceutical companies should add flavoring to their medications to foster ease of medication-taking.

Self-efficacy for medication-taking was unrelated to adherence rates. Other studies have demonstrated a relationship between medication nonadherence and self-efficacy [38] and relatedly perceived autonomy in the management of treatment [56]. It may be that self-efficacy is high early post-transplant and diminishes over time, as does medication adherence, in concert with fewer routine clinic visits and less reinforcement about the importance of medication-taking.

We recommend that transplant centers and nephrologists caring for kidney recipients help kidney recipients strengthen their enabling factors and eliminate barriers to medication-taking. Specifically, transplant clinicians should educate transplant candidates and recipients about potential barriers to medication-taking as well as strategies to foster medication-taking while waiting for a transplant or early post-transplant respectively. Transplant centers and nephrologists should also routinely assess whether kidney recipients encounter new or additional barriers and educate patients about strategies to overcome them. This effort entails a transformation in transplant centers from a short-term to a long-term approach to caring for kidney recipients, which would coincide with the Chronic Care Model.

Future research should assess the effectiveness of strategies for fostering medication-taking and assess patients' willingness and perceived level of ease with which to incorporate them into their daily routine. Patient education interventions sponsored by transplant teams and the pharmaceutical industry designed to improve attitudes about immunosuppressant medication adherence, to promote the use of effective strategies, and to eliminate barriers may foster improved medication-taking. Understanding the range of barriers to medication adherence and strategies to overcome barriers among kidney transplant recipients is important to: (i) increase adherence in the future, (ii) help physicians understand patients' experiences to find possible approaches to overcome barriers, (iii) develop a screening tool to identify patients most likely at risk of engaging in nonadherence, and (iv) design interventions to help prevent nonadherence in the patient population.

There are limitations to our study. First, adherence was measured by self-report, and was not confirmed by an objective measure. Although self-reported nonadherence is generally considered less valid than electronically monitored approaches, it has been shown to be highly reliable when interviews take place in confidential settings, as occurred herein [51]. Additionally, self-reported nonadherence has been found to be significantly related to nonadherence rates using electronic monitoring [11,38]. The measures of adherence used were dichotomous, rather than continuous which has been recently recommended as a more effective approach [8]. Second, the recruitment attrition rate of 43% may have resulted in a biased sample. That the sample was relatively highly educated may be a vestige of characteristics of patients willing to participate in the study. It is also possible that recruitment attrition may be related to poor health which may be correlated with poorer adherence to recommended self-care behaviors. Third, as most patients were interviewed on average 2 months post-transplant, they have had limited experience with the process of reordering refills from the pharmacy; additional issues are likely to emerge as patients interact with pharmacies over time. Relatedly, the high rates of adherence found herein may diminish and the kinds of barriers to medication-taking that patients encounter may change after 3 years post-transplant when Medicare's coverage of immunosuppressants ends. Fourth, as a multi-site study conducted in the Midwest and Northeast, the findings may not be generalizable to other geographic areas in the US. However, no significant differences in adherence levels were found between the two regions.

Conclusion

This paper advances the literature on adherence and medication-taking by identifying barriers that kidney recipients encounter, even while being adherent. Understanding the range of barriers to adherence and strategies kidney recipients devised to promote medication-taking may help transplant providers to better educate transplant candidates and recipients about appropriate medication-taking, and may inform patient-centered interventions to improve medication adherence.

Authorship

EJG: designed research/study, performed research/study, collected data, analysed data, wrote the paper. MG and DC: wrote the paper. ARS and LAS: designed research/study, wrote the paper.

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References

1. Laupacis A, Keown P, Pus N, *et al.* A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996; **50**: 235.
2. Wolfe RA, Ashby VB, Milford EL, *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; **341**: 1725.
3. United Network for Organ Sharing (UNOS)/OPTN. *Number of Kidney Transplants Performed 1997-2007*. Based on OPTN data as of March 14, 2008. [UNOS data request received 3-18-08, UNOS Data Request # 3-13-2008-4] http://www.unos.org
4. United Network for Organ Sharing (UNOS)/OPTN. *Patients Transplanted in the U.S. between October 1, 1987–December 31, 2006 by Organ Received and Most Recent Status*. Based on OPTN data as of September 21, 2007. http://www.unos.org
5. Vlaminck H, Maes B, Evers G, *et al.* Prospective study on late consequences of subclinical non-compliance with immunosuppressive therapy in renal transplant patients. *Am J Transplant* 2004; **4**: 1509.
6. Matas AJ, Humar A, Gillingham KJ, *et al.* Five preventable causes of kidney graft loss in the 1990s: a single-center analysis. *Kidney Int* 2002; **62**: 704.
7. De Geest S, Borgermans L, Gemoets H, *et al.* Incidence, determinants, and consequences of subclinical noncompliance with immunosuppressive therapy in renal transplant recipients. *Transplantation* 1995; **59**: 340.
8. Morrissey PE, Flynn ML, Lin S. Medication noncompliance and its implications in transplant recipients. *Drugs* 2007; **67**: 1463.

9. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999; **47**: 555.
10. Sketris I, Waite N, Grobler K, West M, Geerus S. Factors affecting compliance with cyclosporine in adult renal transplant patients. *Transplant Proc* 1994; **26**: 2538.
11. Schafer-Keller P, Steiger J, Bock A, Denhaerynck K, De Geest S. Diagnostic accuracy of measurement methods to assess non-adherence to immunosuppressive drugs in kidney transplant recipients. *Am J Transplant* 2008; **8**: 616.
12. Takemoto SK, Pinsky BW, Schnitzler MA, *et al.* A retrospective analysis of immunosuppression compliance, dose reduction and discontinuation in kidney transplant recipients. *Am J Transplant* 2004; **7**: 2704.
13. Chisholm MA, Vollenweider LJ, Mulloy LL, *et al.* Renal transplant patient compliance with free immunosuppressive medications. *Transplantation* 2000; **70**: 1240.
14. Denhaerynck K, Desmyttere A, Dobbels F, *et al.* Nonadherence with immunosuppressive drugs: US compared with European kidney transplant recipients. *Prog Transplant* 2006; **16**: 206.
15. Dew MA, Dimartini AF, De Vito Dabbs A, *et al.* Adherence to the medication regimen during the first two years after lung transplantation. *Transplantation* 2008; **85**: 195.
16. Russell C, Conn V, Ashbaugh C. Medication-taking beliefs of adult renal transplant recipients. *Clin Nurse Spec* 2003; **17**: 200.
17. Siegal BR, Greenstein SM. Postrenal transplant compliance from the perspective of African-Americans, Hispanic-Americans, and Anglo-Americans. *Adv Ren Replace Ther* 1997; **4**: 46.
18. Siegal BR, Greenstein SM. Profiles of noncompliance in patients with a functioning renal transplant: a multicenter study. *Transplant Proc* 1999; **31**: 1326.
19. Kory L. Nonadherence to immunosuppressive medications: a pilot survey of members of the transplant recipients international organization. *Transplant Proc* 1999; **31**: 14S.
20. Didlake RH, Dreyfus K, Kerman RH, Van Buren CT, Kahan BD. Patient noncompliance: a major cause of late graft failure in cyclosporine-treated renal transplants. *Transplant Proc* 1988; **20**: 63.
21. Zelikovsky N, Schast AP, Palmer J, Meyers KE. Perceived barriers to adherence among adolescent renal transplant candidates. *Pediatr Transplant* 2008; **12**: 300.
22. Bullington P, Pawola L, Walker R, Valenta A, Briars L, John E. Identification of medication non-adherence factors in adolescent transplant patients: the patient's viewpoint. *Pediatr Transplant* 2007; **11**: 914.
23. Neu AM. Special issues in pediatric kidney transplantation. *Adv Chronic Kidney Dis* 2006; **13**: 62.
24. Butler JA, Peveler RC, Roderick P, Smith PWF, Horne R, Mason JC. Modifiable risk factors for non-adherence to immunosuppressants in renal transplant recipients: a cross-sectional study. *Nephrol Dial Transplant* 2004; **19**: 3144.
25. Siegal BR, Greenstein SM. Compliance and noncompliance in kidney transplant patients: cues for transplant coordinators. *J Transpl Coord* 1999; **9**: 104.
26. Chisholm M, Kwong WJ, Spivey CA. Associations of characteristics of renal transplant recipients with clinicians' perceptions of adherence to immunosuppressant therapy. *Transplantation* 2007; **84**: 1145.
27. Williams AF, Manias E, Walker R. Adherence to multiple, prescribed medications in diabetic kidney disease: a qualitative study of consumers' and health professionals' perspectives. *Int J Nurs Stud* 2008; **42**: 1742.
28. Munger MA, Van Tassell BW, LaFleur J. Medication nonadherence: an unrecognized cardiovascular risk factor. *MedGenMed* 2007; **9**: 58.
29. Bryman A. Quantitative and qualitative research: further reflections on their integration. In: Brannen J, ed. *Mixing Methods: Qualitative and Quantitative Research*. Brookfield, CT: Avebury, 1992: 57–78.
30. Russell CL, Conn VS, Ashbaugh C, Madsen R, Hayes K, Ross G. Medication adherence patterns in adult renal transplant recipients. *Res Nurs Health* 2006; **29**: 521.
31. Bayliss EA, Ellis JL, Steiner JF. Barriers to self-management and quality-of-life outcomes in seniors with multimorbidities. *Ann Fam Med* 2007; **5**: 395.
32. Bury M. The sociology of chronic illness: a review of research and prospects. *Sociol Health Illn* 1991; **13**: 451.
33. Charmaz K. Grounded theory in the 21st century. Applications for Advancing Social Justice Studies. In: Denzin NK, Lincoln YS, eds. *The Sage Handbook of Qualitative Research*. Thousand Oaks, CA: Sage Publications, 2005: 507–535.
34. Leventhal H, Leventhal EA, Contrada RJ. Self-regulation, health, and behavior: a perceptual-cognitive approach. *Psychol Health* 1998; **13**: 717.
35. Bandura A. *Self-efficacy: The Exercise of Control*. New York: Freeman, 1997.
36. Clark NM, Gong M, Kaciroti N. A model of self-regulation for control of chronic disease. *Health Educ Behav* 2001; **28**: 769.
37. Clark NM, Dodge JA. Exploring self-efficacy as a predictor of disease management. *Health Educ Behav* 1999; **26**: 72.
38. Denhaerynck K, Steiger J, Bock A, *et al.* Prevalence and risk factors of non-adherence with immunosuppressant medication in kidney transplant patients. *Am J Transplant* 2007; **7**: 108.
39. Baines LS, Joseph JT, Jindal RM. Compliance and late acute rejection after kidney transplantation: a psycho-medical perspective. *Clin Transplant* 2002; **16**: 69.
40. Creswell JW, Plano Clark VL. *Designing and Conducting Mixed Methods Research*. Thousand Oaks, CA: Sage Publications, 2007.
41. Zyzanski SJ, McWhinney IR, Black R, Crabtree BF, Miller WL. Qualitative research: perspectives on the future. In: Crabtree BF, Miller WL, eds. *Doing Qualitative Research*. Newbury Park: Sage Publications, 1992: 231–248.

42. De Geest S, Abraham I, Gemoets H, Evers G. Development of the long-term medication behaviour self-efficacy scale: qualitative study for item development. *J Adv Nurs* 1994; **19**: 233.
43. Powers WR. *Transcription Techniques for the Spoken Word*. New York: AltaMira Press, 2005.
44. Seidel JV, Kjolseth R, Seymour E. *The Ethnograph: A User's Guide*. Littleton, CO: Qualis Research Associates, 1985.
45. Luborsky M. The identification and analysis of themes and patterns. In: Gubrium JF, Sankar A, eds. *Qualitative Methods in Aging Research*. Thousand Oaks, CA: Sage Publications, 1994: 189–210.
46. Huberman AM, Miles MB. Data management and analysis methods. In: Denzin NK, Lincoln YS, eds. *Handbook of Qualitative Research*. Thousand Oaks, CA: Sage Publications, 1994: 413–427.
47. Bradley EH, Curry LA, Devers KJ. Qualitative data analysis for health services research: developing taxonomy, themes, and theory. *Health Serv Res* 2007; **42**: 1758.
48. Bernard HR, Ryan GW. Text analysis: qualitative and quantitative methods. In: Bernard HR, ed. *Handbook of Methods in Cultural Anthropology*. Walnut Creek, CA: Altamira Press, 1998: 595–646.
49. U.S. Renal Data System. *USRDS 2007 Annual Data Report: Atlas of Chronic Kidney Disease and End-stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2007.
50. Achille MA, Ouellette A, Fournier S, Vachon M, Herbert MJ. Impact of stress, distress and feelings of indebtedness on adherence to immunosuppressants following kidney transplantation. *Clin Transplant* 2006; **20**: 301.
51. Butler JA, Peveler RC, Roderick P, Horne R, Mason JC. Measuring compliance with drug regimens after renal transplantation: comparison of self-report and clinician rating with electronic monitoring. *Transplantation* 2004; **77**: 786.
52. Frazier PA, Davis-Ali SH, Dahl KE. Correlates of noncompliance among renal transplant recipients. *Clin Transplant* 1994; **8**: 550.
53. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther* 2001; **23**: 1296.
54. Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of the literature. *J Behav Med* 2008; **31**: 213.
55. Chisholm MA. Identification of medication-adherence barriers and strategies to increase adherence in recipients of renal transplants. *Manag Care Interface* 2004; **17**: 44.
56. Gremigni P, Bacchi F, Turrini C, Cappelli G, Albertazzi A, Bitti PE. Psychological factors associated with medication adherence following renal transplantation. *Clin Transplant* 2007; **21**: 710.