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Abstract

Medication nonadherence after liver transplantation (LT) is associated with adverse clinical outcomes such as graft rejection and graft loss. Few studies have examined nonadherence and its impact on clinical outcomes in LT. The study objectives were (1) to evaluate medication understanding (with treatment knowledge and demonstrated regimen use scores) and medication adherence or nonadherence to entire regimens among LT recipients and (2) to examine associations of these exposures with clinical outcomes. We conducted a 2-site study of 105 recipients between 2011 and 2012 at 2 transplant centers in Chicago, IL and Atlanta, GA. Data were collected via detailed, in-person interviews and medical record reviews. Study participants were middle-aged and predominantly male; 15% of the sample had limited literacy. On average, patients were taking 11 medications [standard deviation (SD) = 4], and 39% had undergone a medication change within the last month. The average scores for the entire medication regimen were 86% (SD = 22%) for treatment knowledge and 78% (SD = 22%) for demonstrated regimen use. The mean score for self-reported nonadherence to the entire regimen was 14% (SD = 20%).

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Additional Supporting Information may be found in the online version of this article.

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whereas 32% of the patients were nonadherent according to tacrolimus levels. In multivariate analyses, lower income, less time since transplantation, a higher number of medications, and limited literacy were inversely associated with treatment knowledge scores (all \( P < 0.05 \)), whereas limited literacy was associated with nonadherence according to tacrolimus levels \( (P < 0.05) \). In multivariate models, higher scores for treatment knowledge [incidence rate ratio (IRR) = 0.85, 95% confidence interval (CI) = 0.74–0.97] and demonstrated regimen use \( (IRR = 0.87, 95\% \text{ confidence interval} = 0.77–0.98) \) were independently associated with 15% and 13% reductions in the number of posttransplant rehospitalizations, respectively. Inadequate treatment knowledge and improper regimen use may be significant determinants of unintentional nonadherence among LT recipients and are associated with adverse clinical outcomes.

Over the last several decades, advances in surgical techniques and immunosuppression (IS) therapies have resulted in improved survival in solid organ transplantation.\(^1\) However, the effectiveness of optimal IS, in particular, has been hampered by highly complex multidrug regimens that require strict adherence over time.\(^2\)–\(^4\) The scope of the problem is significant because nearly half of late acute rejection episodes and 15% of graft losses in adults are attributed to IS nonadherence.\(^5\)–\(^6\) In kidney transplant recipients, nonadherence has been estimated to cost as much as $33,000 per patient over the course of 3 years after transplantation.\(^7\)

Pooled estimates from the currently available transplant literature indicate that 25% to 30% of solid organ transplant recipients may be nonadherent to IS medications over the course of a year.\(^2\)\(^6\)\(^8\) According to a meta-analysis from 2007 by Dew et al.,\(^2\) low levels of education, nonwhite ethnicity, inadequate social support, and poorer self-reported health were identified as likely risk factors for nonadherence. Although the prevalence and risk factors for nonadherence in transplant recipients have been previously reported, the literature has focused predominantly on kidney transplant patients and suffers from methodological limitations.\(^5\)–\(^10\) Most investigations to date have had small samples, retrospective study designs, limited measures, and variable definitions of nonadherence.\(^2\) Additionally, the extent and nature of medication-related problems among liver transplantation (LT) recipients are less well known.\(^11\)

The purpose of this study was to examine in greater detail the prevalence of LT recipients’ treatment knowledge, demonstrated regimen use, and adherence to their prescribed IS and non-IS medication regimens. In addition, we sought to investigate more comprehensively patient- and regimen-specific risk factors for misuse and nonadherence and to examine associations between these crucial self-care behaviors and transplant-specific outcomes, including posttransplant rehospitalization, graft rejection, and infection.

**PATIENTS AND METHODS**

We conducted in-person, structured interviews and electronic medical record (EMR) data abstraction to examine associations between LT recipients’ treatment knowledge, demonstrated regimen use, medication adherence, and clinical outcomes.
Study Sample

English-speaking LT recipients who were 18 years old or older were recruited from 2 transplant centers in Chicago, IL and Atlanta, GA from December 2011 to December 2012. The EMR at each site was used to identify eligible patients with upcoming transplant clinic appointments. In Chicago, letters were sent to all potentially eligible patients 2 weeks before their follow-up appointment, and this allowed them to opt out of the study. Patients at both sites were reached via telephone and invited to participate in interviews on the same day as their follow-up appointments at the transplant clinic. Exclusion criteria included limited English proficiency; any severe cognitive, hearing, or vision impairment (factors that could preclude participation in structured, in-person interviews); and transplantation within the 30 days. Participation rates were calculated with the American Association for Public Opinion Research standards. Information on the baseline demographics, organ type, and time since transplantation was collected for all eligible patients. Written informed consent was obtained from all participants on the day of the interview. The institutional review board approved the study protocols and procedures at both sites.

Procedure

Trained research assistants performed structured, in-person interviews with study participants, and they lasted for approximately 45 minutes. Collected information included baseline demographic information and assessments of health literacy, cognitive function, social support, treatment knowledge, demonstrated regimen use, and self-reported medication adherence, as described in detail later.

Measurement

A general sociodemographic survey battery was administered to all participants. Social support was measured with the 6-item Lubben Social Network scale. Health literacy was assessed with a brief and validated scale commonly employed in health literacy research: the Newest Vital Sign. Global cognitive function was measured with the Mini-Mental State Examination. Participants were asked to bring all of their medicine bottles to the study interview; in rare cases in which actual medication vials were not available, the current medication list was used to assist the interview. Medications were classified into 3 groups: transplant IS (eg, tacrolimus, sirolimus, prednisone, and mycophenolate mofetil), transplant non-IS (eg, nystatin, valganciclovir, and trimethoprim sulfamethoxazole), and chronic disease medications (eg, antihypertensives and hypoglycemics). Short-duration medications (eg, analgesics and antibiotics) and over-the-counter medications were excluded from the analyses. For each medication, we assessed treatment knowledge, demonstrated regimen use, and medication adherence as described next.

Treatment Knowledge—We determined patients’ knowledge of their prescribed medication regimens by asking participants if they knew the indication for each medication; if they stated yes, they were asked to state it. A treatment knowledge score was calculated by the determination of the mean percentage of correct responses for all medications.

Demonstrated Regimen Use—On the basis of an approach repeatedly used by members of our study team, demonstrated proper use was evaluated by participants demonstrating
exactly how they took each medication. For this task, participants placed beads that represented their pills into a dosing tray with 24 compartments, each compartment representing 1 hour of the day. The participants were able to refer to their pill bottles or medication lists as needed at all times. Assistance by caregivers was not permitted. Demonstrated regimen use scores were calculated for each medication; patients were scored as having answered correctly on the basis of the number of pills per dose, the number of doses per day, and correct spacing. A demonstrated regimen use score was calculated by the determination of the mean percentage of correct demonstrated use for all medications.

**Medication Adherence**—Self-reported adherence was assessed for each medication with the Patient Medication Adherence Questionnaire. Patients were considered nonadherent if they reported having missed 1 or more doses in the past 4 days. Similar to the scores for treatment knowledge and demonstrated regimen use, a mean medication adherence score was calculated for all medications. An additional biological measure of medication adherence was obtained from the EMR with the tacrolimus standard deviation (SD; see the Clinical Data section for details). An SD ≥2.5 µg/dL was considered to indicate nonadherence. Previous studies have shown that a tacrolimus SD ≥2.5 µg/dL is associated with nonadherence and graft rejection.

**Clinical Data**—Trained research assistants obtained clinical information from the electronic health record at both sites. Among patients taking tacrolimus, the SD was calculated from at least 6 outpatient values closest to the interview date. Additional data included baseline clinical characteristics and clinical outcomes such as rehospitalizations (at the transplant center or another institution), biopsy-proven or suspected graft rejection, and infections (documented by microbiology and radiology in the case of pneumonia). The clinical data were obtained from 2 months before the study interview date to 12 months after the interview.

**Analysis Plan**

Descriptive statistics were calculated for each variable. Chi-square analyses were performed to compare categorical variables between groups; t tests and Wilcoxon rank sum tests were performed to compare continuous variables between groups. An analysis of variance was used to compare mean correct scores for each medication category (transplant IS versus transplant non-IS versus chronic disease). Multivariate, linear, logistic, and negative binomial regression models (in cases of overdispersed data) were used to examine associations for the outcomes of treatment knowledge, demonstrated regimen use, and medication adherence as well as clinical outcomes such as rehospitalizations, infections, and graft rejection. Multivariate models for the outcomes of treatment knowledge and medication nonadherence by tacrolimus levels included covariates found to be associated with outcomes with $P < 0.10$ in bivariate analyses as well as baseline characteristics. The model for rehospitalizations included baseline demographics and characteristics previously noted to be associated with the outcome in prior literature as well as those with $P < 0.10$ in bivariate analyses. The model fit was assessed with the Hosmer-Lemeshow statistic and Vuong’s nonnested likelihood ratio tests. Because this was an exploratory investigation, no a
RESULTS

In all, 163 individuals were contacted to participate in the study; 1 was deceased, 9 were ineligible, 32 refused, and 15 could not be interviewed as a result of scheduling conflicts. The final study sample consisted of 105 participants with an overall response rate of 64% and a calculated cooperation rate of 76%. Table 1 shows the baseline demographics and characteristics of the study sample, including demographic information for patients who opted out of the study. No differences were noted by age, sex, race/ethnicity, or time since transplantation between patients who participated and those who opted out of the study. The mean age of the sample was 57 years (SD = 13 years); patients were predominantly male (59%). There was considerable diversity by race/ethnicity and socioeconomic status; 13% were African American, 25% had less than a high school education, and 16% had a household income less than $20,000 per year. A total of 15% of patients had limited literacy. In addition, 12% of patients were identified as having mild cognitive impairment, and 10% reported inadequate social support. The median time period since transplantation was 20 months (interquartile range = 9–59 months).

On average, patients had 1.3 chronic comorbid conditions (SD = 1.0) and were taking an average of 11 daily medications (SD = 4). This included an average of 1.8 IS medications (SD = 1.1), 1.0 non-IS transplant medications (SD = 1.3), 3.7 chronic disease medications (SD = 2.9), and 2.1 over-the-counter products (SD = 2.0). Patients within 12 months of transplantation were taking significantly more medications than patients farther out from transplantation [mean: 12.2 (SD = 4.3) versus 9.1 (SD = 4.0), P < 0.001].

Table 2 demonstrates the mean scores for the outcomes of treatment knowledge, demonstrated regimen use, medication adherence, and clinical outcomes. On average, patients knew the indication for 86% (SD = 22%) of all their medications. This translated to knowing 90% (SD = 24%) of their transplant IS indications, 73% (SD = 38%) of transplant non-IS indications, and 85% (SD = 26%) of chronic disease medications. The mean demonstrated regimen use score was 78% (SD = 22%) for all medications, 66% (SD = 38%) for transplant IS medications, 76% (SD = 37%) for transplant non-IS medications, and 84% (SD = 24%) for chronic disease medications. By self-report, participants were nonadherent to 14% (SD = 20%) of their medications, 8% (SD = 22%) of transplant IS drugs, 22% (SD = 34%) of transplant non-IS medication, and 15% (SD = 21%) of chronic disease medications. Roughly one-third (32%) of patients were nonadherent according to tacrolimus levels (ie, they had an outpatient tacrolimus SD ≥2.5 µg/dL).

Nearly half (49%) of patients had a posttransplant rehospitalization. The most common reasons for hospitalization (as shown in Table 3) were infection/fever (30%); medical complications such as renal failure and cardiopulmonary and gastrointestinal complications (28%); and postsurgical complications such as wound infections and biliary strictures (20%). Suspected or confirmed graft rejection accounted for 6% of rehospitalizations. Overall, 10%
of patients experienced an episode of suspected or confirmed graft rejection, and 30% of patients had an infection; not all episodes resulted in hospitalization.

In bivariate analyses of the outcomes of treatment knowledge and nonadherence by the biological measure (the results are detailed in Supporting Table 1), limited literacy was associated with lower treatment knowledge scores and nonadherence by the biological measure (tacrolimus SD ≥ 2.5 µg/dL). An annual household income < $50,000, transplantation within 12 months, and a higher number of medications were all associated with lower treatment knowledge scores. No significant associations were noted between covariates and the outcomes of demonstrated regimen use and nonadherence by self-report.

Multivariate results for the outcomes of treatment knowledge and medication adherence by the biological measure are shown in Table 4. Factors independently associated with lower treatment knowledge scores were an annual income < $50,000 [β = −11.9, confidence interval (CI) = −20.4 to −3.5], fewer than 12 months since transplantation (β = −13.2, CI = −22.4 to −4.1), and limited literacy (β = −8.6, CI = −18.3 to −1.1). The presence of limited literacy (odds ratio = 3.8, CI = 1.1–22.1) was independently associated with higher odds of medication nonadherence by the biological measure (tacrolimus SD ≥ 2.5 µg/dL).

As shown in Table 2, rejection episodes were rare (10%), whereas infections (38%) and rehospitalizations (49%) were more common. With the exception of the time since transplantation, no covariates were noted to have significant associations with graft rejection or infection; therefore, multivariate analyses were not carried out for these outcomes. Table 5 displays the multivariate results for the outcome of the number of rehospitalizations. After adjustments for the baseline demographics and characteristics, time since transplantation, literacy level, treatment knowledge, and demonstrated regimen use, higher scores on the treatment knowledge [incidence rate ratio (IRR) = 0.85, 95% CI = 0.74–0.97] and demonstrated regimen use tasks (IRR = 0.87, 95% CI = 0.77–0.98) were independently associated with 15% and 13% reductions, respectively, in the number of posttransplant rehospitalizations. The nonadherence covariates (measured by self-report and tacrolimus SD levels) did not show significant associations with the number of rehospitalizations in bivariate analyses, did not significantly change the magnitude of effect estimates, and did not improve the model fit, so they were not included in the final models.

**DISCUSSION**

To our knowledge, this is the first study to investigate medication-taking behavior and to comprehensively evaluate regimen adherence and its impact on clinical outcomes for LT recipients. In addition, our study identifies health literacy, knowledge of medication indications, and the ability to demonstrate proper dosing as factors that could affect posttransplant self-care. The investigation was conducted at 2 sites and with a large, ethnically and sociodemographically diverse sample. Our findings confirm that LT recipients take exceptionally complex multidrug regimens and experience frequent medication changes. We also found that a significant proportion of recipients were unable to identify the indication for the majority of their medications and could not demonstrate proper dosing of their entire drug regimen. Nonadherence (measured by self-report and tacrolimus SD) was
also significantly prevalent in our study sample. The lower prevalence of nonadherence reported by patients versus that obtained with the biological measure is not surprising; it has previously been shown that patients tend to underestimate nonadherence. The noted discordance between the 2 measures confirms the challenges of accurately capturing nonadherence and suggests the need to assess globally additional aspects of medication-taking behavior to evaluate patients’ ability to effectively manage multidrug regimens.

A summary statement from the 2009 consensus conference on nonadherence in transplantation highlighted substantial challenges in accurately assessing adherence in solid organ transplant recipients. We have attempted to address some of these difficulties by comprehensively exploring the sociodemographic, cognitive, and clinical risk factors for medication misunderstanding and nonadherence in transplantation. We found that a lower annual income, transplantation within 12 months, a greater number of medications, and limited literacy were independently associated with lower treatment knowledge. Transplant recipients taking a greater number of medications and those with limited literacy were more likely to be nonadherent as measured by tacrolimus trough levels.

Establishing health literacy as a potential risk factor for poorer medication self-management in transplantation may have important implications for clinical practice. Health literacy encompasses an individual’s ability to interface effectively with the health-care environment, and limited literacy affects approximately 80 million US adults. In the general chronic disease population, multiple studies have linked limited literacy to worse clinical outcomes such as poor diabetic control, medication nonadherence, and increased hospitalizations and mortality. In transplantation, in which medication regimens are very complex and patients may have significant comorbidities, interventions to address health literacy disparities may decrease rehospitalizations and could improve posttransplant outcome. These strategies could include tools to decrease complexity and increase care coordination through simplified patient instructions, enhanced medication labels, additional counseling, and periodic monitoring and feedback for at-risk patients.

Rather than measuring only missed or incorrect doses, our investigation is the first to our knowledge to extensively assess patients’ understanding of their entire medication regimen and to study the associations between treatment knowledge, demonstrated regimen use, and clinical outcomes. Although previous studies have reported associations between IS nonadherence and late acute rejection, our findings suggest that patients’ understanding and use of their entire regimen are critical and may reduce the risk for posttransplant rehospitalization in LT recipients. Thus, the routine assessment of a patient’s understanding of the prescribed IS and non-IS regimen and not only adherence via conventional methods may be warranted to identify at-risk patients earlier and prevent adverse events. Furthermore, we recommend that future medication-adherence interventions in transplant recipients examine additional outcomes beyond graft rejection, such as adverse medication events, side effects, costs, infections, and hospitalizations.

This study has several limitations. Although our research addresses important gaps about medication-taking behavior and clinical outcomes in a large, diverse sample of transplant recipients, our sample may be subject to a recruitment bias from convenience sampling.
Patients who participated in interviews might have represented a more motivated group, and this may have potentially led us to underestimate the rates of medication misunderstanding, nonadherence, and adverse clinical outcomes. However, no significant differences were noted in demographics or the time since transplantation between patients who participated in the study and those who opted out. Self-reported nonadherence may have underestimated the true prevalence, but this was a pilot study, and more robust adherence measurements (eg, electronic monitors or pharmacy refill records) were not employed because of cost; these methods should be used in future prospective trials. Because of sample size limitations, we were likely unable to adequately examine associations with graft rejection and infection; these outcomes should be explored in larger prospective trials. As a result of the exploratory nature of this study and the cross-sectional approach, we cannot claim that medication knowledge outcomes directly resulted in an increased number of hospitalizations and can only more broadly comment on the noted associations. There was no accounting for medical comorbidities, which could have increased the risk of rehospitalization; this information should be collected as part of larger prospective trials. The approach to rejection treatment and monitoring was not protocolized; IS doses may have been increased for possible rejection in cases when biopsies were not performed, and this may have possibly underestimated the incidence of rejection. The role of caregivers in medication-taking behavior was not examined, and this may have possibly overestimated the prevalence of medication misunderstanding if a patient’s spouse or loved one was more responsible for such tasks. Future studies should be performed to assess caregiver involvement, knowledge, and outcomes in the posttransplant population. Finally, we used theoretical scenarios and a dosing exercise instead of observing actual patient behavior. It is possible that patients performed better when they were taking their actual medication regimens or in front of the interviewers.

We have identified important sociodemographic, cognitive, and clinical factors that may predispose LT recipients to medication misunderstanding, nonadherence, and adverse clinical outcomes. Although the problem of IS nonadherence has previously been described in transplantation, this is the first study in the field to measure patients’ knowledge and demonstrated use of their entire medication regimens. Our results additionally show that knowledge of one’s medications and demonstrated proper ability are associated with a lower likelihood of rehospitalization, and this highlights potentially modifiable risk factors and targets for future interventions. The clinical relevance of medication-understanding assessments is that they may expand the number of patients at risk for unintentional nonadherence and adverse outcomes resulting from confusion over medication. In addition to prospectively validating the aforementioned relationships, multifaceted and cost-effective interventions with existing transplant center resources are warranted in order to improve patients’ ability to manage complex drug regimens properly in order to improve long-term posttransplant outcomes.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.
Acknowledgments

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Abbreviations

- **CI**: confidence interval
- **EMR**: electronic medical record
- **IRR**: incidence rate ratio
- **IS**: immunosuppression
- **LT**: liver transplantation
- **REALM**: Rapid Estimate of Adult Literacy in Medicine
- **SD**: standard deviation

References

### TABLE 1
Baseline Sociodemographic and Clinical Characteristics of LT Recipients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Participated (n = 105)</th>
<th>Opted Out (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>57 (13)</td>
<td>57 (14)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>43 (41)</td>
<td>21 (36)</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>14 (13)</td>
<td>6 (10)</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>85 (81)</td>
<td>42 (72)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (6)</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Transplant within 12 months, n (%)</td>
<td>48 (46)</td>
<td>16 (28)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>26 (25)</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>42 (40)</td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>37 (35)</td>
<td></td>
</tr>
<tr>
<td>Yearly household income, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$20,000</td>
<td>16 (16)</td>
<td></td>
</tr>
<tr>
<td>$20,000-$50,000</td>
<td>27 (27)</td>
<td></td>
</tr>
<tr>
<td>&gt;$50,000</td>
<td>59 (58)</td>
<td></td>
</tr>
<tr>
<td>Limited literacy (REALM), n (%)</td>
<td>15 (15)</td>
<td></td>
</tr>
<tr>
<td>Mild cognitive impairment, n (%)</td>
<td>11 (12)</td>
<td></td>
</tr>
<tr>
<td>Inadequate social support, n (%)</td>
<td>10 (10)</td>
<td></td>
</tr>
<tr>
<td>Months since transplant, median (interquartile range)</td>
<td>20 (9–59)</td>
<td></td>
</tr>
<tr>
<td>Number of chronic conditions, mean (SD)</td>
<td>1.3 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Number of medications, mean (SD)</td>
<td>11 (4)</td>
<td></td>
</tr>
</tbody>
</table>

* Race was missing for 4 patients.
† Income, literacy information were available among n = 102, and cognitive function information available on n = 95.
### TABLE 2

Treatment Knowledge, Demonstrated Regimen Use, Nonadherence, and Clinical Outcomes Among LT Recipients (n = 105)

<table>
<thead>
<tr>
<th></th>
<th>Treatment knowledge (%)</th>
<th>Demonstrated regimen use (%)</th>
<th>Nonadherence by self-report (%)</th>
<th>Rehospitalization, n (%)</th>
<th>Rejection, n (%)</th>
<th>Infection, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td>mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All medications</td>
<td>86 ± 22</td>
<td>78 ± 22</td>
<td>14 ± 20</td>
<td>51 (49)</td>
<td></td>
<td>40 (38)</td>
</tr>
<tr>
<td>Transplant IS</td>
<td>90 ± 24</td>
<td>66 ± 38</td>
<td>8 ± 22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transplant non-IS</td>
<td>73 ± 38</td>
<td>76 ± 37</td>
<td>22 ± 34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic disease</td>
<td>85 ± 26</td>
<td>84 ± 24</td>
<td>15 ± 21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonadherence by biological measure (tacrolimus SD ≥2.5 µg/dL)</td>
<td>27 (32)</td>
<td>27 (32)</td>
<td>27 (32)</td>
<td>27 (32)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Treatment knowledge indicates correctly identified indications for all medications, demonstrated regimen use indicates correctly demonstrated dosing during the interview, and nonadherence by self-report indicates the mean percentage of nonadherence to all medications within the past 7 days (score of 0 = perfect adherence).

* Complete data were available for 57 patients.
### TABLE 3

**Primary Reason for Hospitalization Among LT Recipients**

<table>
<thead>
<tr>
<th>Hospitalization Reason</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection/fever</td>
<td>36 (30)</td>
</tr>
<tr>
<td>Medical complication</td>
<td>34 (28)</td>
</tr>
<tr>
<td>Postsurgical complication</td>
<td>24 (20)</td>
</tr>
<tr>
<td>Graft rejection (suspected or confirmed)</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Other</td>
<td>20 (17)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>121</strong></td>
</tr>
</tbody>
</table>

NOTE: *Medical complication* indicates renal failure, electrolyte abnormalities, or cardiopulmonary or gastrointestinal symptoms; *postsurgical complication* indicates a wound infection/abscess, biliary complication, or incisional hernia.
TABLE 4
Multivariate Results for the Outcomes of Treatment Knowledge and Nonadherence by Biological Measure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment Knowledge (Mean Percentage Correct)</th>
<th>Nonadherence by Biological Measure (Tacrolimus SD ≥2.5 µg/dL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Annual income (&lt;$50,000 versus ≥$50,000)</td>
<td>−11.9 (−20.4 to −3.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Months since transplant (≤12 versus &gt;12)</td>
<td>−13.2 (−22.4 to −4.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Number of medications</td>
<td>−1.0 (−2.1 to 0.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Literacy on REALM (limited versus adequate)</td>
<td>−8.6 (−18.3 to −1.1)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

NOTE: The model for the outcome of treatment knowledge includes covariates with P < 0.10 in bivariate analyses; the model for the outcome of nonadherence by the biological measure includes the same covariates included in the previous model for ease of interpretation.

* Data are reported for 57 patients with complete tacrolimus data.
### TABLE 5
Multivariate Results for the Outcome of the Number of Hospitalizations Among LT Recipients

<table>
<thead>
<tr>
<th>Variable</th>
<th>IRR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 versus &lt;65 years</td>
<td>0.73</td>
<td>0.36–1.46</td>
<td>0.37</td>
</tr>
<tr>
<td>Male</td>
<td>1.24</td>
<td>0.68–2.26</td>
<td>0.49</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>0.84</td>
<td>0.36–1.95</td>
<td>0.68</td>
</tr>
<tr>
<td>Time since transplant ≤12 months</td>
<td>0.83</td>
<td>0.44–1.56</td>
<td>0.56</td>
</tr>
<tr>
<td>Limited literacy (REALM)</td>
<td>0.69</td>
<td>0.29–1.60</td>
<td>0.38</td>
</tr>
<tr>
<td>Treatment knowledge (mean %) *</td>
<td>0.85 *</td>
<td>0.74–0.97</td>
<td>0.02</td>
</tr>
<tr>
<td>Demonstrated regimen use (mean %)*</td>
<td>0.87 *</td>
<td>0.77–0.98</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**NOTE:** The model includes baseline demographics and covariates with \(P < 0.10\) in bivariate analyses.

*The effect estimate is reported for each 10% increase in treatment knowledge and demonstrated use scores.*