Emotional Functioning, Barriers, and Medication Adherence in Pediatric Transplant Recipients

Megan L. McCormick King,[1] PhD, Laura L. Mee,[2] PhD, Ana M. Gutiérrez-Colina,[3] BA,
Cyd K. Eaton,[3] BS, Jennifer L. Lee,[3] MS, and Ronald L. Blount,[3] PhD

[1]Department of Psychiatry and Behavioral Sciences, Children's National Medical Center, Washington, DC,
[2]Transplant Program, Department of Pediatrics, Children's Healthcare of Atlanta and Emory University School
of Medicine, Atlanta, GA, and [3]Department of Psychology, University of Georgia, Athens, GA

All correspondence concerning this article should be addressed to Megan L. McCormick King, PhD,
Department of Psychiatry and Behavioral Sciences, Children's National Medical Center, 111 Michigan Ave
NW, Suite 3600, Washington, DC 20010, USA. E-mail: mmccormi@cnmc.org

Objective This study assessed relationships among internalizing symptoms, barriers to medication adherence, and medication adherence in adolescents with solid organ transplants. **Method** The sample included 72 adolescents who had received solid organ transplants. Multiple mediator models were tested via bootstrapping methods. **Results** Bivariate correlations revealed significant relationships between barriers and internalizing symptoms of depression, anxiety, and posttraumatic stress, as well as between internalizing symptoms and medication adherence. Barriers indicative of adaptation to the medication regimen (e.g., forgetting, lack of organization) were related to medication adherence and mediated the relationship between internalizing symptoms and medication adherence. **Conclusions** These findings indicate that barriers may serve as a more specific factor in the relationship between more general, pervasive internalizing symptoms and medication adherence. Results may help guide areas for clinical assessment, and the focus of interventions for adolescent transplant recipients who are experiencing internalizing symptoms and/or who are nonadherent to their medication regimen.

Key words adherence; adolescents; anxiety; chronic illness; depression; health behavior; organ transplantation; posttraumatic stress.

Introduction

Solid organ transplantation has become the standard of care and a desirable treatment option for many pediatric kidney, heart, and liver conditions. Although prognoses have improved (Horslen, Barr, Christensen, Ettenger, & Magee, 2007) and life spans have lengthened, receiving a solid organ transplant is a trade from a life-threatening illness to a chronic health condition that requires ongoing maintenance throughout the life span. Among the most important activities required to maintain the life and health of a transplanted organ is strict adherence to complex medication regimens, in particular to immunosuppressant medications (Rianthavorn, Ettenger, Malekzadeh, Marik, & Struber, 2004).

Unfortunately, medication adherence in pediatric populations is suboptimal and even poorer during adolescence, a time when adherence rates tend to decrease (DiMatteo, 2004). For adolescent transplant recipients, medication nonadherence may be as prevalent as 43% (Dobbels et al., 2010), with adolescents demonstrating significantly higher nonadherence than young children (Dew et al., 2009). Potential consequences of nonadherence to medications by transplant recipients include higher health care costs, hospitalization, rejection episodes, allograft loss, and death (Falkenstein, Flynn, Kirkpatrick, Casa-Melley, & Dunn, 2004). In addition, poor adherence can lead to difficult decision-making by health care providers regarding the allocation of scarce organs to previously

nonadherent patients (Cleemput, Kesteloot, & De Geest, 2002; Harmon, Lefante, & Krousel-Wood, 2006). Understanding the interplay of factors that influence nonadherence is a needed focus for research and a critical step for promoting patient health, high-quality care, and improved medical outcomes.

Research has examined numerous potential barriers associated with intentional or nonintentional medication nonadherence, including forgetfulness (Gray, Denson, Baldassano, & Hommel, 2012), issues with time management (Bregnballe, Schiotz, Boisen, Pressler, & Thastum, 2011), regimen complexity (Hommel & Baldassano, 2010), and beliefs about medication ineffectiveness or treatment undesirability (Chisholm, 2002; Rhee, Belyea, Ciurzynski, & Brasch, 2009). Simons and Blount (2007) developed the Adolescent Medication Barriers Scale (AMBS), a multidimensional factor-analytically derived measure, to assess barriers to medication adherence in pediatric transplant recipients. In addition to finding significant relationships between more barriers and less adherence in a cross-sectional sample, a subsequent 18-month longitudinal investigation showed that these barrier domains tended to be relatively stable over time and predictive of future nonadherence and negative clinical outcomes, including more hospitalizations, rejection episodes, and death (Simons, McCormick, Devine, & Blount, 2010).

Pediatric transplant recipients experience increased levels of emotional difficulties, such as anxiety, depression, and posttraumatic stress symptoms (PTSS), relative to their healthy peers or peers with other chronic health conditions (e.g., Berney-Martinet et al., 2009; Fredericks, Lopez, Magee, Shieck, & Opipari-Arrigan, 2007; Mintzer et al., 2005). For example, Fredericks et al. (2007) found that based on parent proxy-report on the Child Behavior Checklist, ~60% of transplant recipients scored in the clinical range for Internalizing and/or Externalizing problems, Total Problems, or at least one subscale, as compared with only 25–30% in the normative sample. Another study with pediatric liver transplant recipients found that 32% of the sample met criteria in all three domains of posttraumatic stress disorder (PTSD), including reexperiencing of the medical trauma, avoidance, and hyperarousal (Shemesh et al., 2000). Higher levels of these general emotional difficulties also have been linked to poor adherence in a variety of patient populations, including youth with organ transplants (e.g., Fredericks et al., 2007; Gray et al., 2012; Maikranz, Steele, Dreyer, Stratman, & Bovaird, 2007).

Despite our knowledge that both barriers and emotional distress are related to adherence, no studies to date have examined the interrelationships of these variables in youth with organ transplants. Questions remain as to what mechanisms or intermediary factors play a role in the relationship between emotional distress and medication adherence. Answering these questions can have important implications for patient management and health care professionals, as they respond to nonadherence in adolescents with chronic illnesses. Therefore, the current study examined the relationships between adolescent internalizing symptoms, barriers, and medication adherence, as well as the mediational role of barriers in the relationship between internalizing symptoms and medication adherence. Consistent with the aforementioned literature findings, we hypothesized that greater internalizing symptoms of anxiety, depression, and PTSS, as well as higher levels of each of the three AMBS subscales (i.e., Regimen Adaptation/Cognitive Issues [RA/CIs], Disease Frustration/Adolescent Issues [DF/AIs], and Ingestion Issues [IIs]), would be associated with less medication adherence. Additionally, we hypothesized that greater internalizing symptoms would be associated with more barriers. Finally, we predicted that perceived barriers to adherence would be a mediating factor in the relationship between internalizing symptoms and medication adherence.

Method
Participants

The current sample included 72 adolescent solid organ (i.e., kidney, liver, heart) transplant recipients. Inclusion criteria required participants to speak English and to be at least 6 months posttransplant to allow for stabilization in medical care and adherence behaviors. Patients with significant developmental delays, as indicated by prior evaluation or parent report, were excluded. Of the 76 eligible patients approached for participation, four patients declined due to lack of interest, resulting in a participation rate of 95%.

Participants were aged from 12 to 21 years ($M = 17.8$, $SD = 2.45$), were 56% male, and were 60% Caucasian, 30% African American, and 10% other races/ethnicities. Thirty-seven participants (51%) were kidney recipients, 27 (38%) were liver recipients, 5 (7%) were heart recipients, 2 participants (3%) had both kidney and heart transplants, and 1 participant (1%) had both liver and kidney transplants. Time since transplant ranged from 6 months to 18 years ($M = 6.7$, $SD = 5.03$ years).

Measures

Barriers to Adherence
Participants completed the AMBS (Simons & Blount, 2007), which assesses adolescents' perceived barriers to

medication adherence. This 17-item scale asks respondents to rate barriers on a 5-point Likert scale from "*strongly disagree*" to "*strongly agree*." There are three factor-analytically derived subscales: RA/CI (e.g., "I am not very organized about when and how to take the medication"; five items), DF/AI (e.g., "I do not want other people to notice me taking the medication"; eight items), and II (e.g., "I have a hard time swallowing the medication"; four items). For the current study, Cronbach's alpha for the AMBS Total Barriers score was .86, RA/CI was .81, DF/AI was .75, and II was .55, indicating strong internal consistency for all scales except IIs. Given that the II subscale was derived through factor analysis and has been associated with salient clinical outcomes in previous investigations including hospitalizations and mortality (Simons et al., 2010), this subscale was retained in analyses despite its lower reliability to capture this unique and important facet of barriers.

Emotional Functioning

Adolescent emotional functioning was assessed in three domains of internalizing symptoms: Depression, anxiety, and PTSS. Symptoms of anxiety and depression were assessed using the Behavior Assessment System for Children- 2nd Edition Self Report of Personality, Adolescent Version (BASC-2-SRP-A; Reynolds & Kamphaus, 2004) and Anxiety and Depression Subscales. Internal consistency for this sample was .89 for the Anxiety subscale and .88 for the Depression subscale. T-scores were calculated based on age and gender norms and used in the subsequent analyses. Additionally, PTSS were assessed using a revised version of the Child PTSD Symptoms Scale (CPSS; Foa, Johnson, Feeny, & Treadwell, 2001). Participants were specifically prompted at the top of the questionnaire to briefly describe their most distressing event "in relation to [their] experience with medical diagnosis, transplant surgery, and ongoing medical care" to direct their attention specifically to medical experiences. Participants were then instructed to complete the subsequent questions based on the distressing medical event that they identified. The 17 items assessing total symptom severity were used to calculate a total symptom score. Internal consistency for this scale was high, with $\alpha = .94$.

Medication Adherence

To assess medication adherence, adolescents completed the Medication Adherence Measure (MAM; Zelikovsky & Schast, 2008; Zelikovsky, Schast, Palmer, & Meyers, 2008), a brief semistructured interview that assesses adherence to prescribed medications. The MAM has shown good convergent validity, with a systematic review of adherence (Dobbels et al., 2010) reporting that higher rates of nonadherence on the MAM were positively correlated with rates of nonadherence calculated with electronic monitoring (e.g., Medication Event Monitoring Systems). Nonadherence reported with the MAM has also been associated with barriers to adherence and clinical outcomes, such as organ rejection 2 years posttransplant (Simons et al., 2010; Zelikovsky et al., 2008).

Medications assessed with the MAM included both immunosuppressants and any other medications (e.g., steroids, antihypertensives, vitamins) that were prescribed by the participant's physician as part of their medical regimen. Participants reported on the number of doses of each medication that were missed or taken late in the 7 days before study participation. "Late" doses were defined as any medication taken >30 min past the scheduled/prescribed time. Percentages of missed and late doses were calculated by dividing the total number of missed or late doses by the total number of prescribed doses in the previous 7 days.

Procedure

Potential participants were recruited at a major pediatric transplant center during regularly scheduled outpatient clinic appointments. Informed consent from caregivers and assent from youth was obtained for youth aged <18 years. For participants aged >18 years, consent was directly obtained from the adolescent. Data collection occurred in conjunction with the medical appointment. Adolescent participants completed all self-report questionnaires while in the waiting room or in the clinic room between visits by members of a multidisciplinary team. The brief semistructured adherence interview subsequently was conducted by a trained member of the research staff in the patient's clinic room. If a parent was present, they were asked to leave the room for the interview portion of the assessment. Data collection lasted ~30 min, and participants were compensated with a $10 gift card. All study procedures were approved by the Institutional Review Board of participating institutions.

Data Analysis

Pearson product moment correlations and one-way analyses of variance (ANOVAs) were used in preliminary analyses. Pearson correlations also were conducted to examine the bivariate relationships among the primary variables of interest. Bootstrapping techniques were used to examine indirect effects using an SPSS macro outlined by Preacher and Hayes (2004, 2008; available online at http://www.afhayes.com/spss-sas-and-mplus-macros-and-code.html). Bootstrapped estimations of the indirect effect are based on

5000 iterations and produce a 95% confidence interval (CI) for that estimate. The indirect effect is determined to be significantly different from zero and therefore significant, if zero does not fall within the CI. Six models were tested. For those models, the three AMBS subscales were used as mediators. The Total Barriers variable was not included because of the overlap of information between the subscales and total scale.

Results
Preliminary Analyses

Means and standard deviations for all variables are included in Table I. No significant differences were present for gender, race, and type of transplant, and no signficant assocations were present for age and time since transplant, when compared with scores on the AMBS (Total or

Table I. *Descriptive Information for Primary Variable*

Measure	N	Mean	SD	Range
Barriers to adherence				
AMBS				
Total	72	33.65	11.03	17–62
RA/C	72	7.16	2.85	4–14
DF/AI	72	17.22	6.30	8–32
II	72	9.15	2.92	5–18
Emotional functioning				
BASC anxiety (T score)	72	43.00	10.24	29–73
BASC depression (T score)	72	47.71	11.53	39–88
CPSS total	72	8.10	10.51	0–45
Medication adherence				
% Meds missed	72	4.23	12.64	0–95
% Meds late	72	11.49	20.48	0–100

Note. RA/C = regimen adaptation/cognitive; DF/AI = disease frustration/adolescent issues; II = ingestion issues; CPSS = Child Posttraumatic Stress Scale; % Meds missed = percentage of medication doses missed in last 7 days; % Meds late = percentage of medication doses taken late in past 7 days; BASC is standardized with a mean of 50 and a standard deviation of 10.

subscales) and the number of missed or late medications. There was a significant gender difference for the BASC Anxiety subscale (F [1, 70] = 4.734, p = .033), with girls (M = 45.4, SD = 11.5) scoring higher than boys on average (M = 40.3, SD = 7.9). Similarly, girls (M = 50.3, SD = 12.7) scored significantly higher than boys (M = 44.8, SD = 9.4) on the BASC Depression subscale (F [1, 70] = 4.304, p = .042). Because of these differences, gender was used as a covariate in subsequent mediational analyses using Anxiety and Depression subscales. No significant differences were found for PTSS based on demographic factors.

Rates of Emotional Distress

Means, standard deviations, and ranges of scores for the three domains of emotional functioning are detailed in Table I. For depessive symptoms, four participants (5.5%) had scores in the "at risk" range (T-score from 60 to 69), and five participants (6.9%) fell in the "clinically significant" range (T-score >70). For symptoms of anxiety, five participants (6.9%) had scores in the "at risk" range, and one participant (1.4%) fell in the "clinically significant" range. For PTSS, 19 participants (26.4%) had scores ≥11, the originally established clinical cutoff score for the CPSS (Foa et al., 2001).

Correlational Results

Correlations were conducted between total barriers and barriers subscales, indices of emotional functioning, and measures of adherence (Table II). To sum, total barriers and the three barrier subscales were significantly and positively correlated with the emotional domains of anxiety, depression, and PTSS, with the exception of the relationship between IIs and PTSS, which was not significant. Further, symptoms of anxiety, depression, and posttraumatic stress were positively correlated with percentages of missed medication doses. Measures of emotional

Table II. *Correlation Matrix for All Variables*

Measure	BASC anx	BASC dep	CPSS	AMBS total	RA/CI	DF/AI	II
AMBS							
Total	.47**	.48**	.43**	–	–	–	–
RA/CI	.40*	.63**	.44**	–	–	–	–
DF/AI	.45*	.56**	.31*	–	–	–	–
II	.33**	.22	.28*	–	–	–	–
% Meds missed	.26*	.26*	.26*	.21	.30*	.11	.08
% Meds late	.21	.18	.17	.39**	.37**	.31**	.23

Note. RA/C = regimen adaptation/cognitive; DF/AI = disease frustration/adolescent issues; II = ingestion issues; BASC anx = BASC anxiety subscale; BASC dep = BASC depression subscale; CPSS = Child Posttraumatic Stress Scale; % Meds missed = Percent of medication doses missed in past 7 days; % Meds late = percentage of medication doses taken late in past 7 days.

*p < .05, **p < .01.

functioning were not significantly correlated with late medication doses. Finally, RA/CIs were positively correlated with missed medication doses, and higher Total Barriers, RA/CIs, and DF/AIs were associated with a greater percentage of late medication doses.

Mediation Analyses

Figure 1 illustrates the total and indirect effects of the mediation model for anxiety, barriers, and missed medication doses. As shown in the figure, only RA/C barriers mediated the relationship between symptoms of anxiety and percentage of missed medication doses, with a point estimate of .24 ($SE = .20$; 95% CI .03–1.02). The direct effect of anxiety on missed doses became less significant ($t = 2.07$, $p = .04$) with the inclusion of the mediating variable, in comparison with the direct effect without the mediating variable ($t = 2.60$, $p = .01$), indicating partial mediation. The total model accounted for 20% of the variance in self-reported adherence, $R^2 = .20$, $p < .01$. In this model, gender also served as a significant covariate ($t = -2.01$, $p = .048$).

Similarly, and as illustrated in Figure 2, RA/C barriers mediated the relationship between symptoms of depression and percentage of missed medication doses, with a point estimate of .23 ($SE = .18$; 95% CI .03–.97). The direct effect of depressive symptoms on missed doses became nonsignificant ($t = 1.78$, $p = .08$) with the inclusion of the mediating variable, in comparison with the direct effect without the mediating variable ($t = 2.63$, $p = .01$), indicating

full mediation. The total model accounted for 19% of the variance in self-reported adherence, $R^2 = .19$, $p = .01$.

As shown in Figure 3, RA/C barriers also mediated the relationship between PTSS and percentage of missed medication doses, with a point estimate of .22 ($SE = .19$; 95% CI .02–1.03). The direct effect of PTSS on missed doses became nonsignificant ($t = 1.33$, $p = .19$) with the inclusion of the mediating variable, in comparison with the direct effect without the mediating variable ($t = 2.21$, $p = .03$), indicating full mediation. The total model accounted for 14% of the variance in self-reported adherence, $R^2 = .14$, $p = .03$.

No significant mediators were detected in the relationship between internalizing symptoms and late medication doses.

Discussion

The current study examined the relationships among facets of emotional functioning, barriers to medication adherence, and medication adherence in youth with solid organ transplants. We expected internalizing symptoms and barriers to be both positively correlated and related to increased nonadherence. We also expected that perceived barriers to adherence would serve as medication-specific factors mediating the relationship between emotional functioning and medication adherence. Findings were partially consistent with our hypotheses, and the results of the study contribute to the literature
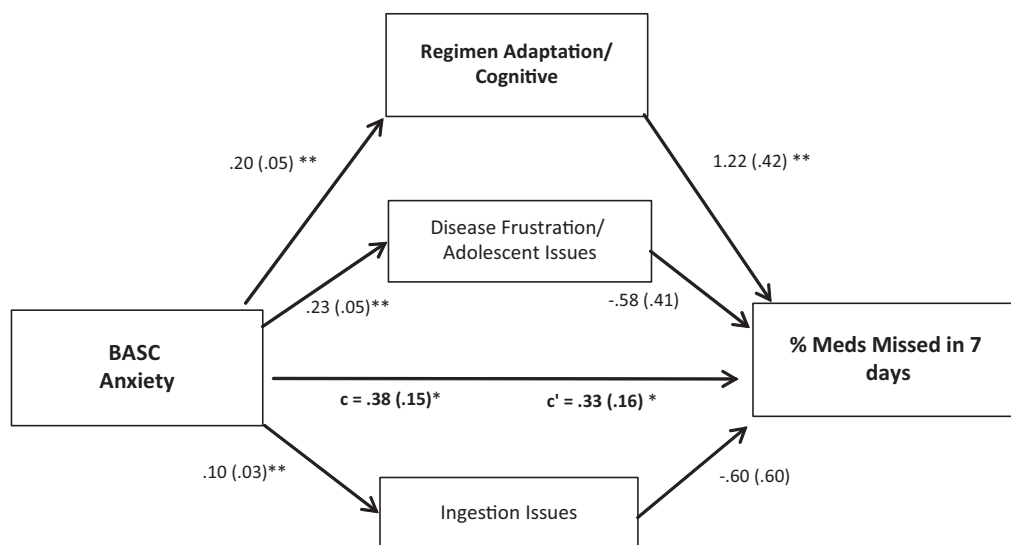

Figure 1. Mediation model: RA/C barriers mediate the relationship between anxiety symptoms and missed medication doses. *Note.* Path values represent unstandardized regression coefficients. Standard errors are noted in parentheses. BASC = Behavior Assessment System for Children. *c* represents the initial relationship between the independent variable and the outcome variable. *c′* represents the direct effect of the independent variable on the outcome variable when the mediator is present. **p < .05, ** p < .01.*
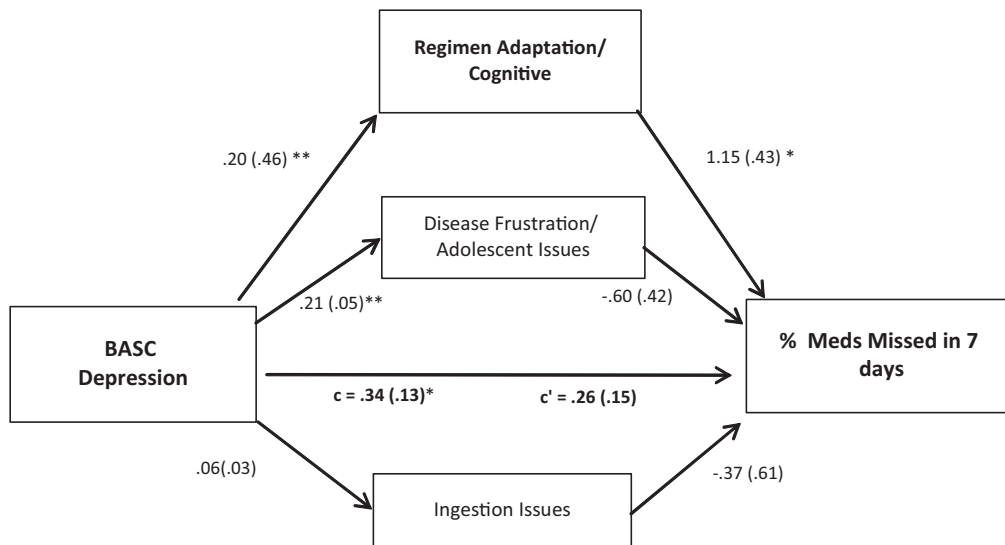
Figure 2. Mediation model: RA/C barriers mediate the relationship between depressive symptoms and missed medication doses. *Note.* Path values represent unstandardized regression coefficients. Standard errors are noted in parentheses. BASC = Behavior Assessment System for Children. *c* represents the initial relationship between the independent variable and the outcome variable. *c′* represents the direct effect of the independent variable on the outcome variable when the mediator is present. *p < .05, **p < .01.
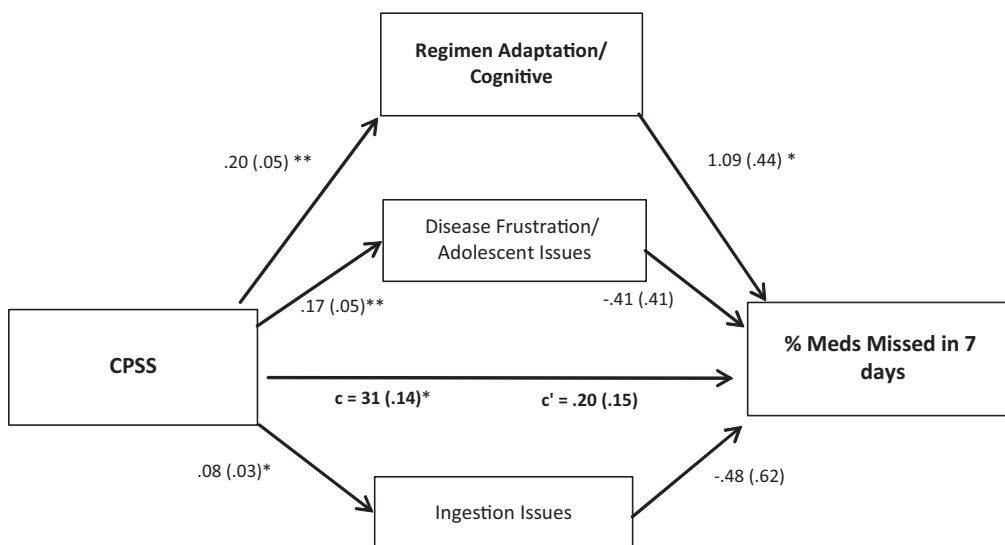

Figure 3. Mediation model: RA/C barriers mediate the relationship between PTSSs and missed medication doses. *Note.* Path values represent unstandardized regression coefficients. Standard errors are noted in parentheses. CPSS = Child Posttraumatic Stress Scale. *c* represents the initial relationship between the independent variable and the outcome variable. *c′* represents the direct effect of the independent variable on the outcome variable when the mediator is present. *p < .05, **p < .01.

by shedding light on the relationships among these three important patient factors.

As reported in previous investigations (Simons et al., 2010), patients who endorsed more barriers also had poorer adherence to their medications. Endorsing more RA/C barriers (e.g., lacking organization, not planning ahead) was associated with higher rates of missed

medication doses. Further, patients who endorsed a greater degree of Total, RA/CIs, and DF/AIs (e.g., being tired of taking medications, not wanting friends to notice) were more likely to take medications late.

These results suggest that RA/C barriers were more salient for missing medications than other types of barriers, whereas being late in taking medication is associated with

a wider variety of barriers. It is possible that some DF/AI barriers involve avoidance or active resistance that delays medication administration, but owing to the more visible nature of these barriers (e.g., expressing frustration with medications), caregivers or other adults are cued to increase supervision or encourage the patient's eventual medication taking. In contrast, RA/C barriers primarily involve a failure to think proactively, such as not planning ahead, not refilling prescriptions on time, or lacking organization in medication management. It is possible that these types of barriers are less obvious to others and occur inadvertently, allowing for fewer prompts to correct one's actions.

Although not measured in the current study, it is also possible that caregiver characteristics played a role in this differential finding between barrier type and missed or late medication-taking. Whereas DF/AIs may be specific to adolescents' feelings about their disease and may be detected and modified by an adult with a different perspective toward the disease, planning and organization issues could also be experienced by caregivers and pervasive throughout a family. Thus, RA/C barriers may be less likely to be identified and compensated for by caregivers who experience similar issues.

IIs were not associated with medication adherence. This may be due to adolescents endorsing disagreement or strong disagreement that IIs barriers were a problem ($M = 1.83$), thus creating a floor effect and restricted range of scores. Further, the low endorsement and thus, low reliability of this particular factor may have contributed to this subscale's inability to capture previously reported relationships with outcome measures (e.g., Simons et al., 2010). It is also possible that even though severe IIs occur at a low rate, thus adversely affecting internal consistencey, IIs may have a significant influence on adherence if present. Further exploration of the reliability and validity of the IIs subscale will be important to determine if our findings are particular to this sample.

Also consistent with our hypothesis, adolescents with more symptoms of depression, anxiety, and posttraumatic stress were more likely to miss medication doses. Overall, these findings are consistent with other investigations indicating that greater depressive symptoms (Maikranz et al., 2007), higher levels of anxiety (Embry, 2003; Turner, Williams, Sloan, & Haselkorn, 2009), and more emotional problems (i.e., anger; Penkower et al., 2003) are associated with poorer adherence to medications. A small number of studies have reported no significant associations between psychosocial difficulties (i.e., depression or anxiety) and increased risk for nonadherence in pediatric transplant recipients (Fredericks et al., 2007; Penkower

et al., 2003). A recent study with pediatric transplant recipients also described positive associations between anxiety symptoms and adherence but reported that adherence rates generally declined over time (Wu, Aylward, & Steele, 2010). Wu et al. (2010) attributed these unexpected results to a number of potential explanatory factors, such as strong reactivity effects to ongoing electronic medication monitoring. To our knowledge, there is only one other study in children with cystic fibrosis that mirrored results of Wu et al. (White, Miller, Smith, & McMahan, 2009).

Given that the lack of literature to contextualize these conflicting findings, the results of the current study may be more representative of the literature, overall. It also is well established that emotional distress is related to poorer daily functioning (American Psychiatric Association, 2000). For internalizing symptoms in pediatric populations, these symptoms may relate to impaired motivation, increased negative cognitions about one's situation, and/or interference with attention and concentration necessary to carry out successful disease management, all of which could be conceptualized as risk factors for nonadherence. In support of this idea, the current study also showed that higher levels of anxiety, depression, and PTSSs are associated with more barriers to medication adherence, indicating that barriers may be a specific factor in the larger relationship between internalizing symptoms in children's day-to-day life and the factors that may be more specifically related to medication adherence.

To formally investigate this hypothesis and advance our understanding of the relationships between these three important variables, mediation analyses were conducted. We reasoned that in the relationship between internalizing symptoms and adherence, internalizing symptoms may play a general and pervasive role in this relationship, whereas barriers would represent a more situation-specific manifestation of those difficulties as they relate to adherence. Three models involving each facet of emotional functioning were significant and showed medium effect sizes. In addition, RA/CIs barriers subscale was significantly associated with missed doses in each of the three analyses. Only RA/CIs mediated the relationships between internalizing symptoms (depression, anxiety, and PTSS) and missed medication doses. Gender emerged as a statistically significant covariate for the partially mediated anxiety model. When gender was excluded from this model, there was full mediation. These findings suggest that removing variance associated with gender improved the accuracy of this model that would otherwise have underestimated the direct contribution of anxiety and overestimated the indirect contribution of RA/CIs to predicting medication nonadherence. Anxiety may be an

enduring predictor of medication nonadherence above and beyond gender-based differences.

Although assumptions about directionality cannot be made due to the cross-sectional nature of this investigation (Maxwell & Cole, 2007), these models do suggest that RA/CIs barriers act as a unique factor in the relationship between internalizing symptoms and adherence. These findings are also reflective of those found in two recent studies in which cognitive barriers (e.g., ''When there are changes to my regimen I sometimes get confused'') mediated the relationship between family support and disease control in adolescents with asthma (Rhee, Belyea, and Brasch, 2010), and RA/CIs on the AMBS mediated the relationship between externalizing symptoms and medication adherence in youth with gastrointestinal disorders (Reed-Knight, Lewis, & Blount, 2013). The consistency of these investigations with the current study's results supports the use of this particular model, as well as the salience of cognitive barriers in the relationship between psychosocial factors and medication adherence.

This study not only provides preliminary evidence to expand our understanding of adherence and helps guide future research but also has potential clinical implications for pediatric healthcare providers. First, barriers measures are a useful tool with which to understand more about medication nonadherence in pediatric patients. Patients may benefit from interventions to reduce barriers. Also, the presence of emotional factors may cue clinicians to examine for barriers that may interfere with medication adherence. Further, it is possible that some patients experiencing barriers related to lack of planning and organization may benefit from interventions that go beyond specific medication-related prompting to address broader more pervasive factors at play, including internalizing symptoms. It is possible that reducing internalizing symptoms with evidence-based interventions may subsequently result in reduced barriers and improved medication adherence.

Limitations to this study should be noted. As stated earlier in the text, our ability to draw conclusions about causality is limited due to the cross-sectional nature of this research. The current study does, however, serve as a first step in uncovering some unique and specific factors, like cognitive barriers, that mediate the relationship between emotional functioning and adherence. Second, these findings are based on individual self-report, which may pose the risk of inaccuracy due to poor recall or social desirability. It is possible that adolescents may have under-reported nonadherence, even though the MAM relies on a shorter period of recall to increase accuracy, and some literature has suggested that adolescent report of adherence may be

more clinically valid than the reports of their caregivers (Simons et al., 2010). This study also was conducted at a transplant center where adherence-promoting interventions are delivered on an ongoing basis. As such, caution should be taken when generalizing these findings to other groups. The use of more objective measures of adherence (e.g., laboratory values) and the expansion of research to include additional sites and additional reporters (e.g., parents) would increase the generalizability of the findings across patients and geographical locations.

We also note that in the current sample, rates of clinically significant depressive (6.9%) and anxiety (1.4%) symptoms appeared to be lower than those reported for other pediatric groups (e.g., Ekinci, Titus, Rodopman, Berkmen, & Trevathan, 2009; Katon et al., 2007). Rates of clinically significant PTSSs (20.8–26.4%), in contrast, appeared to be at the upper end of what would be expected in the overall population of pediatric transplant recipients, which ranges from 11 to 21% (Mintzer et al., 2005; Ingerski, Shaw, Gray, & Janicke, 2010; Walker, Harris, Baker, Kelly, & Houghton, 1999; Wallace et al., 2004). Despite these discrepancies, results of the aforementioned mediation models show that varying levels of internalizing symptoms may have a salient relationship with barriers and adherence.

There are a number of additional directions for future research in this area. In response to the aforementioned limitations, findings from this study should be replicated within a longitudinal context and should include additional forms of data (e.g., parent proxy) and measures of health outcomes. Future research also should investigate the roles of additional predictive factors such as externalizing behavior problems and/or neurocognitive factors (e.g., executive dysfunction), both of which may also give rise to particular barriers and thereby impact adherence (McNally, Rohan, Pendley, Delamater, & Drotar, 2010). Additionally, studies investigating the associations among emotional states, barriers, and adherence should be extended to additional pediatric populations for whom medication adherence is problematic. Finally, future research should investigate the associations between adolescents' emotional factors, barriers, and adherence to different prescribed mediations by pharmacists (e.g., immunosuppressants, corticosteroids, antihypertensives) and to prescribed medictions that are bought over-the-counter (Reed-Knight, Lewis, & Blount, 2010).

In sum, the results of the current study provide further insight into the relationships between emotional factors and specific barriers that are associated with poorer adherence. In particular, the presence of clinical and subclinical levels of internalizing symptoms should be assessed,

acknowledged, and addressed, given the possible negative relationship to medication adherence. Adolescence is a distinctive time in life that poses specific challenges, which are often accentuated for those with serious medical conditions. Professionals working in this area must maintain a wholistic view of these young patients, conceptualizing their nonadherence in the context of the multiple factors that inevitably influence their self-management behaviors.

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