Patient Health Beliefs and Characteristics Predict Longitudinal Antihypertensive Medication Adherence in Adolescents With CKD

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Abstract

Objective To investigate longitudinal associations of health beliefs, which included self-efficacy, outcome expectancies, and perceived barriers, and demographic risk factors (i.e., age, gender, race, and family income) with antihypertensive medication adherence in adolescents with chronic kidney disease (CKD) over 24 months. **Method** The sample included 114 adolescents (M age = 15.03 years, $SD = 2.44$) diagnosed with CKD. Adolescents reported their self-efficacy for taking medications, medication outcome expectancies, and barriers to adherence at baseline and 12 and 24 months after baseline. Antihypertensive medication adherence was assessed via electronic monitoring for 2 weeks at baseline and 6, 12, 18, and 24 months after baseline. **Results** Adherence increased and then decreased over the 2-year study period (inverted U-shape). Self-efficacy, outcome expectancies, and barriers did not change over time. Older adolescent age, female gender, African American race, <\$50,000 annual family income, and public health insurance were associated with lower adherence. However, family income was the primary demographic risk factor that predicted adherence over time ($\geq$ \$50,000 annual family income was longitudinally associated with higher adherence). Higher self-efficacy and more positive and less negative outcome expectancies across time were also associated with higher antihypertensive medication adherence across time. **Conclusions** Clinical interventions should be developed to target medication self-efficacy and outcome expectancies to improve long-term antihypertensive medication adherence in adolescents with CKD. Family income may be considered when conceptualizing contextual factors that likely contribute to adolescents' consistent challenges with medication adherence over time.

Key words: adherence; chronic illness; health behavior.

Results of the ESCAPE trial showed that targeting lower blood pressure with antihypertensive medications delayed progression of chronic kidney disease (CKD) in children even without a hypertension diagnosis (Wuhl, Mehls, & Schaefer, 2004; The ESCAPE Trial Group,

2009). More recently, elevated baseline blood pressure in children with CKD was associated with faster glomerular filtration rate (eGFR) decline over time (Warady et al., 2015), which is a major risk factor for end-stage renal disease (ESRD; Coresh et al., 2014), the

final stage of CKD. Children who progress to ESRD are typically treated with dialysis or kidney transplantation (McDonald & Craig, 2004); preserving kidney function with renal protective antihypertensive medications may prevent the need for more invasive and involved treatment options. However, children and adolescents with CKD often present with nonadherence across medication classes, including antihypertensive medications, with nonadherence rates ranging from 6% to 50% when assessed via self-report (Blydt-Hansen et al., 2014). Ongoing clinical challenges with nonadherence have been reported in adolescents with CKD, resulting in postponed active listings for kidney transplantation when needed (Hashim, Vadnais, & Miller, 2013). These findings suggest that a portion of adolescents with CKD may not experience expected health benefits of taking antihypertensive medication because of nonadherence.

Adolescence is a developmental phase associated with greater medication nonadherence compared with younger children (DiMatteo, 2004). Adherence in childhood and adolescence is considered a dynamic behavior that may change or decrease over time (Modi, Rausch, & Glauser, 2011; Smith, Mara, & Modi, 2018), necessitating consistent monitoring from providers and families. Adolescents who are prescribed chronic daily treatment regimens may benefit from empirically supported strategies that enhance long-term adherence. An enriched understanding of longitudinal associations between potential predictors of and barriers to adherence is needed to inform the development of such interventions (Annett, 2017).

The social cognitive theory (SCT; Bandura, 2004), a well-established theory of health promotion, provides a framework for conceptualizing how modifiable health beliefs may be targeted to improve long-term adherence. The SCT proposes that adherence is maintained through a strong sense of self-efficacy, the expectation that positive outcomes will occur by following treatment regimens, and fewer obstacles to adherence. In prior pediatric samples, including adolescents with kidney transplants, higher levels of self-efficacy (MacDonell, Jacques-Tiura, Naar, Fernandez, & ATN 086/106 Protocol Team, 2016), more positive and less negative beliefs about adherence outcomes (Hilliard, Eakin, Borrelli, Green, & Riekert, 2015), and fewer barriers (Simons & Blount, 2007) were associated with higher adherence. Lower levels of self-efficacy, more negative perceptions and beliefs about adherence, and more barriers were longitudinally associated with lower adherence and more negative health outcomes in children and adolescents with type 1 diabetes (Fortenberry et al., 2014), solid organ transplant (Simons, McCormick, Devine, & Blount, 2010), and epilepsy (Ramsey, Zhang & Modi, 2018). A prior study showed that barriers to adherence did not

change over two time points in adolescents with solid organ transplants (Lee et al., 2014); however, this study did not investigate if barriers and adherence were associated over time. Further research is needed to evaluate longitudinal associations of health beliefs on adherence in adolescents with CKD.

To comprehensively model longitudinal associations between health beliefs and adherence, the role of demographic risk factors (e.g., age and gender), especially those associated with health disparities (e.g., socioeconomic status [SES] and race), should be considered. The literature generally indicates that older age (DiMatteo, 2004), minority race (Naar-King et al., 2013), and lower SES (Caccavale, Weaver, Chen, Streisand, & Holmes, 2015) are associated with lower adherence or greater disease activity in pediatric patients. Male gender is often considered a risk factor for nonadherence (Naar-King et al., 2006), but findings on gender-based adherence differences are mixed (Modi et al., 2011; Quittner et al., 2014). In children with high-risk conditions (epilepsy and diabetes), lower SES, older age, and ethnic minority backgrounds were associated with lower adherence and disease management over time (Aylward, Rausch, & Modi, 2015; Helgeson et al., 2018; Hilliard, Wu, Rausch, Dolan, & Hood, 2013). Adolescents' beliefs, barriers, and perceptions about their illness and treatment have shown longitudinal associations with adherence beyond the effects of age, gender, or SES (Fortenberry et al., 2014; Smith et al., 2018). Increasing self-efficacy and positive beliefs about adherence while reducing barriers may improve adherence and mitigate the negative impact of certain demographic risk factors.

There is a growing literature on associations between modifiable treatment targets, demographic risk factors, and adherence among children with medical conditions. However, studies have often been cross-sectional or limited to two time points, included subjective adherence assessments, or sampled younger children rather than adolescents. To date, no studies have been conducted to assess the unique adherence challenges for adolescents with CKD using an objective adherence assessment. Hence, the current study aimed to investigate the longitudinal associations of health beliefs, including self-efficacy, outcome expectancies, and barriers, and demographic risk factors with electronically monitored antihypertensive medication adherence in adolescents with CKD over 24 months. Based on the literature, we hypothesized that (a) adherence would decrease over time, (b) self-efficacy and positive outcome expectancies would decrease over time with adherence, while negative outcome expectancies and barriers would increase over time with adherence, and (c) lower self-efficacy, more negative and less positive outcome expectancies, more barriers, and the presence of demographic risk factors

(i.e., older age, male gender, minority race, and lower family income) would be associated with lower adherence over time. These data have scientific and clinical relevance to pediatric psychologists and other providers aiming to improve long-term adherence in adolescents with CKD and potentially other adolescents taking chronic daily medications.

Methods

Procedures

Participants were recruited from three pediatric nephrology clinics at three academic medical centers in the mid-Atlantic United States. All study procedures received institutional review board approval from each site before recruitment. Eligible participants were between the ages of 11 and 19 years at consent with a physician diagnosis of CKD (Stages 1–5) and currently prescribed an antihypertensive medication for >6 months. Exclusion criteria included having a sibling participating in the study, being unable to comprehend spoken English, having a developmental delay precluding completion of study procedures, and an unwillingness to use electronic medication monitoring devices during the study. Potential participants were screened for eligibility from patient rosters at each clinic before being contacted by trained research assistants via telephone to invite them to enroll in the study. If they agreed to join the study, written informed consent or assent was obtained during the first study visit at adolescents' homes or at a family-preferred location (e.g., the clinic).

At baseline, adolescents and caregivers reported on family demographic information. Adolescents completed surveys to assess their self-efficacy for taking medication, medication outcome expectancies, and barriers to adherence at baseline and at 12 and 24 months after baseline; adolescents were prompted to respond to these surveys with regard to prescribed antihypertensive medications. Surveys were administered via audio-enhanced computer-assisted self-interviewing, which involves participants listening to prerecorded surveys on a computer and responding to items on the screen; this method helps reduce literacy demands associated with self-report surveys. Objective antihypertensive medication adherence was measured over 2 weeks at baseline and 6, 12, 18, and 24 months after baseline. Care teams were blinded to participants' levels of adherence during the study. Adolescents received monetary compensation each time they completed surveys and electronic adherence monitoring.

Survey Measures

Demographic and Medical Information

Adolescents and caregivers (for adolescents ≤ 18 years old) reported on family demographic information

(e.g., adolescent race and gender and annual family income). Adolescents' medical information was abstracted from the electronic medical record, including whether they had a hypertension diagnosis in addition to CKD and creatinine levels obtained 6 months before and after baseline. If an adolescent did not have creatinine values available during this time, they were categorized as "Unavailable during study timeframe." Creatinine levels were used to calculate adolescents' estimated eGFRs with the updated Bedside CKiD equation ($0.413 \times \text{height}/\text{creatinine}$; Schwartz et al., 2009) to determine CKD disease stage.

Medication Self-Efficacy

Adolescents' levels of self-efficacy for taking their antihypertensive medications in different situations were assessed with the Riekert Self-Efficacy Scale, which included 12 items adapted from an existing, validated, measure for adults with cystic fibrosis (Eakin et al., 2017). Items were selected and worded to be appropriate for use with adolescents with CKD. Adolescents rated each of the 12 items on a 10-point Likert scale ranging from *Not at all sure* to *Completely sure* (e.g., "How sure are you that you can take your blood pressure medicine the way your doctor said when you are in a hurry?"). To obtain a mean score ranging from 1 to 10, item ratings were summed and divided by 12. Higher scores indicate greater self-efficacy for taking medications. In the current study, internal consistency for the scale ranged from $\alpha = .93$ to $.97$ across the multiple measurement time points.

Positive and Negative Outcome Expectancies

The Beliefs About Medication Scale (BAMS) assessed adolescents' beliefs about antihypertensive medication adherence behaviors (Riekert & Drotar 2002). Although the BAMS contains four subscales, only the Positive Outcome Expectancies (POE, 20 items) and Negative Outcome Expectancies (NOE, 13 items) subscales were analyzed. The POE (e.g., "I have a lot to gain from taking my medicine the way the doctor says I should") and NOE (e.g., "If I take my medicine the way the doctor says I should, it makes me feel sicker") assess adolescents' expectations of favorable or unfavorable outcomes of taking their medications as prescribed. Adolescents rated items on a seven-point Likert scale ranging from *Definitely do not agree* to *Definitely do agree*. Higher scores on the POE reflect more positive expectations and higher scores on the NOE reflect more negative expectations. To obtain mean POE and NOE scores ranging from 1 to 7, item ratings were summed and divided by the number of scale items. In the current study, internal consistency ranged from $\alpha = .83$ to $.87$ on the POE and $\alpha = .86$ to $.87$ on the NOE across the multiple measurement time points.

Barriers to Adherence

The 17-item Adolescent Medication Barriers Scale (AMBS; [Simons & Blount 2007](#)) was used to assess adolescents' perceived barriers to taking antihypertensive medications as prescribed (e.g., "I am not very organized about when and how to take the medication"). Adolescents rated items using a five-point Likert scale ranging from *Strongly disagree* to *Strongly agree*. Although the AMBS has subscales, only the Total score, which is the sum of the 17 items, was analyzed. To enhance interpretability of results, the Total score was divided by 17, resulting in a mean score ranging from 1 to 5. Higher AMBS Total scores indicate more barriers. The AMBS was validated with adolescents with solid organ transplants, including kidney ([Simons et al., 2010](#)). In the current study, internal consistency for the Total score ranged from $\alpha = .89$ to $.92$ across the multiple measurement time points.

Objective Antihypertensive Medication Adherence

Daily antihypertensive medication adherence was measured over 2 weeks at baseline and 6, 12, 18, and 24 months after baseline (five observations total) using the Medication Event Monitoring System (MEMS 6) TrackCap monitors (AARDEX Ltd. Union City, CA). The MEMS TrackCap is a child-resistant medication bottle cap that records the date and time of each bottle opening and closure, which is uploaded through a communicator to a computer. The research team extracted a current medication regimen plan from adolescents' electronic medical records to verify the name of the antihypertensive medication and the frequency and strength of dose per day; this medication regimen was verified for accuracy with the treating physician. During study visits, research assistants placed the MEMS cap on adolescents' antihypertensive medication bottles and conducted a pill count at the start and end of the 2-week observation period as a validity check. Adherence was calculated as the number of doses recorded as "taken" on the MEMS divided by the total number of expected openings based on the prescribed regimen and the number of days in the observation period; this calculated value is then reported as a percentage. If adolescents were prescribed more than one antihypertensive medication, each medication was monitored with a separate bottle and MEMS cap and adherence calculations reflected all medications monitored.

Analytic Plan

For hypothesis testing, statistical significance was inferred when $p < .05$. Descriptive statistics were obtained for the primary study variables (i.e., M , SD , and range) at each measurement point. Pearson

product-moment correlations were used to examine intermeasure associations for adherence, self-efficacy, outcome expectancies, and barriers over time, as well as baseline adolescent age and average adherence (i.e., the average of all available MEMS cap adherence measurements per participant). Demographic differences on average adherence were examined by adolescent gender (male and female), race (African American, Caucasian, Other), annual household income ($< \$50,000$, $\$50,000$ – $\$99,999$, and $\geq \$100,000$), insurance status (private and public), CKD stage (Stages 1–5), and the presence or absence of a hypertension diagnosis using independent samples t -tests and Cohen's d effect size (two group comparisons) or one-way analysis of variance and effect size ω^2 (≥ 3 group comparisons); adolescents categorized with "Not reported" or "Unavailable" demographic data were excluded from these analyses.

Using PROC MIXED (SAS 9.4 Software, Cary, NC, USA), linear mixed models with restricted maximum likelihood estimation and autoregressive covariance structure were used to assess changes in adherence, self-efficacy, outcome expectancies, and barriers over time and to investigate the influence of demographic risk factors (i.e., baseline adolescent age, gender, race, and family income) and time varying self-efficacy, outcome expectancies, and barriers on adherence across 24 months. Demographic risk factors were selected a priori based on variables identified in the literature as related to nonadherence in adolescents ([Aylward et al., 2015](#); [Hilliard et al., 2013](#); [Naar-King et al., 2006](#)). Family income was included in the models rather than health insurance because it is a commonly used indicator of SES ([Cheng, Goodman, & The Committee on Pediatric Research, 2015](#)). Linear mixed models accounted for the expected interindividual correlation between repeated assessments and allowed for retaining adolescents with some missing data. A priori sensitivity analyses were used to evaluate potential patterns in adherence missingness, as some adolescents ($n = 15$) had their antihypertensive medication discontinued by their treating nephrologists and potentially restarted by their physicians at later time points during the 2-year observation period. Results of these sensitivity analyses showed that similar associations were observed between key study variables when including and excluding adolescents with discontinued medications; thus, to maximize the generalizability of our results, these adolescents were retained in final analyses. To assess changes in adherence, self-efficacy, outcome expectancies, and barriers over time, each variable was separately modeled with a subject-level random intercept and a random slope for time as a linear or quadratic effect to account for expected individual variability. AIC values were evaluated to select the best fitting

Figure 1. Consort diagram of participant screening, recruitment, enrollment, and inclusion in final analyses.

model; if the difference in Akaike information criterion (AIC) was <2 (Hilbe, 2011), the more parsimonious random intercept fixed slope model was retained.

To predict adherence over time, self-efficacy, outcome expectancies, and barriers were entered in three separate models as time varying main effects (i.e., values for each time point were included) with an interaction term between the predictor and time. The decision to enter each predictor in a separate model was because of expected high intercorrelations between self-efficacy, outcome expectancies, and barriers as well as the sample size. In each model, baseline adolescent age, gender, race, and family income were entered as demographic covariates. This analytic plan is similar to approaches used in prior pediatric research examining longitudinal associations between beliefs, barriers, and adherence (Fortenberry et al., 2014; Ramsey et al., 2018).

Results

Recruitment and Characteristics of the Study Sample

During recruitment, 130 adolescents with CKD consented to join the study, of which 2 were excluded because of screen failure, for a total of 128 participants. There were no significant differences on age, race, or gender between adolescents who participated ($N = 128$) versus those who declined ($N = 134$).

Of the 128 adolescents who participated, 120 completed electronic antihypertensive medication monitoring at baseline and surveys on at least one occasion.

Of those 120 adolescents, 6 did not report on family income and were excluded from final analyses, as complete income data were needed to appropriately conduct the analytic plan; there were no differences on age, race, or gender between adolescents included in the final sample versus excluded. The final analyzed sample included 114 adolescents with CKD (M age at baseline = 15.03 years, $SD = 2.44$, range = 11–20 years), of which only 3 refused to continue participating at any point during the study duration. See Figure 1 for more details on participant screening, recruitment, enrollment, and inclusion for final analyses. The majority of the sample completed adherence assessments at all five data collection time points (61%; $n = 69$); the average number of adherence assessments completed was 4.25 ($SD = 1.14$). The primary reason for not completing an adherence assessment was the participant no longer took an antihypertensive medication at that time point (6 months: $n = 6$; 12 months: $n = 8$; 18 months: $n = 10$, 24 months: $n = 14$). There were no demographic differences (i.e., age, race, gender, income, insurance type, CKD stage, number of antihypertensive medications prescribed at baseline, and hypertension diagnosis) between participants who completed all five adherence assessments versus those who did not complete ≥ 1 postbaseline adherence assessment.

In the final analyzed sample ($N = 114$), the majority of adolescents were male, African American, had Stages 1–3 CKD, and took one antihypertensive medication. The majority of adolescents took antihypertensive medication once-a-day (79%, $n = 90$), followed

Table I. Sample Demographic Information

Demographic factor	% (n)	Average adherence (%) M (SD)	Test statistic	Effect size
Gender				
Male	54 (61)	78.74 (15.01)	$t = 2.45^*$	$d = .45$
Female	46 (53)	69.21 (25.74)		
Race				
African American	43 (49)	65.95 (22.81) ^{a, b}	$F = 7.61^{**}$	$\omega^2 = .10$
Caucasian	40 (46)	79.85 (18.47) ^a		
Other	17 (19)	82.45 (15.11) ^b		
Annual household income				
<\$50,000	37 (42)	64.38 (25.49) ^{a, b}	$F = 8.53^{***}$	$\omega^2 = .12$
\$50,000–99,999	29 (33)	78.36 (15.68) ^a		
≥\$100,000	34 (39)	81.57 (15.65) ^b		
Health insurance				
Public	40 (45)	68.34 (25.00)	$t = -2.24^*$	$d = -.44$
Private	50 (57)	77.76 (17.51)		
Not reported	10 (12)	–		
Number of antihypertensive medications prescribed at baseline				
1	73 (83)	78.38 (19.31)	$F = 1.93$	$\omega^2 = .02$
2	22 (25)	67.04 (25.84)		
3–4	5 (6)	76.00 (21.12)		
CKD stage				
1	19 (22)	76.75 (20.17)	$F = 0.13$	$\omega^2 = -.03$
2	28 (32)	73.03 (22.80)		
3	22 (25)	74.62 (22.41)		
4–5	12 (14)	75.08 (22.29)		
Unavailable during study time frame	18 (21)	–		
Hypertension diagnosis				
Yes	40 (46)	77.51 (21.93)	$t = -1.33$	$d = .25$
No	60 (68)	72.14 (20.48)		

Note. N = 114. The race category, Other, includes Asian/Pacific Islander (n = 6), Multiracial (n = 8), and Other race (n = 5). *Average Adherence* is the average of each adolescents' adherence (MEMS) across the five possible measurement points. For Race and Annual household income, corresponding superscript letters denote the presence of statistically significant mean differences between categories. For interpreting Cohen's *d*, .20 is "small," .50 is "medium," and .80 is "large." For interpreting ω^2 , .01 is "small," .06 is "medium," and .14 is "large." MEMS = Medication Event Monitoring System.

* $p < .05$, ** $p < .01$, *** $p < .001$.

by twice-a-day (20%, $n = 23$), and three times-a-day (1%, $n = 1$). Less than half of the sample had a documented diagnosis of hypertension. Adolescents were diverse in terms of reported family income and over half had private health insurance. See Table I for detailed demographic information.

Descriptive data for the primary study variables, including the *M*s and *SD*s for adherence, self-efficacy, positive and negative outcome expectancies, and barriers, appear in Table II. The samples' adherence rates ranged from a high of 78.73% doses taken (6 months) to a low of 67.94% doses taken (24 months).

Correlations Between Adherence, Self-Efficacy, Outcome Expectancies, and Barriers

Antihypertensive medication adherence was significantly and positively correlated across time with effect sizes ranging from small to large ($r_s = .39$ to $.65$). Self-efficacy was significantly correlated within-measure across time ($r_s = .40$ to $.65$); similar within-measure correlations were observed for positive ($r_s = .45$ to $.72$) and negative outcome expectancies ($r_s = .65$ to $.80$)

and barriers ($r_s = .58$ to $.76$) with effect sizes ranging from medium to large (Tables III and IV).

Mean Adherence Differences Based on Demographic Risk Factors

Older baseline adolescent age was significantly associated with lower average adherence (i.e., average of each adolescent's adherence across the five possible measurement time points; $r = -.23$, $p = .01$). Males had significantly higher average adherence than females ($d = .45$), African American adolescents had significantly lower average adherence than Caucasians and adolescents of Other racial backgrounds ($\omega^2 = .10$), and adolescents with public health insurance had significantly lower average adherence than those with private health insurance ($d = -.44$); all effect sizes were medium. Adolescents with a household income of <\$50,000 had significantly lower average adherence than adolescents with reported household incomes of \$50,000–\$99,999 and ≥\$100,000, with a medium effect size ($\omega^2 = .12$). There were no statistically significant differences on average adherence

Table II. Descriptive Data for Primary Study Variables

Variable	M (SD)	Range	n
% Antihypertensive medication adherence (MEMS cap)			
Baseline	78.01 (23.11)	4.55–100	114
6 months	78.73 (25.47)	11.11–100	96
12 months	78.45 (27.13)	1.05–100	98
18 months	72.27 (29.87)	2.96–100	91
24 months	67.94 (27.89)	5.00–100	86
Medication self-efficacy			
Baseline	8.16 (1.79)	2.92–10.00	112
12 months	8.27 (1.79)	3.33–10.00	99
24 months	8.44 (1.87)	1.00–10.00	86
Positive outcome expectancies			
Baseline	5.70 (.79)	3.90–7.00	112
12 months	5.62 (.95)	2.05–7.00	99
24 months	5.72 (.89)	2.40–6.90	86
Negative outcome expectancies			
Baseline	2.41 (1.16)	1.00–6.08	112
12 months	2.33 (1.08)	1.00–5.15	99
24 months	2.30 (1.11)	1.00–5.08	86
Barriers to adherence			
Baseline	2.42 (.76)	1.00–4.59	105
12 months	2.31 (.75)	1.00–4.24	99
24 months	2.24 (.83)	1.00–4.12	86

Note. Medication self-efficacy, positive and negative outcome expectancies, and barriers to adherence scores have been scaled to enhance interpretability. Higher scores on medication self-efficacy and positive outcome expectancies indicate higher self-efficacy and positive outcome expectancies; higher scores on negative outcome expectancies and barriers indicate higher negative outcome expectancies and barriers. MEMS = Medication Event Monitoring System.

Table III. Associations Between Antihypertensive Medication Adherence Across 24 Months

	Baseline	6 months	12 months	18 months
Baseline	–			
6 months	.64*** n = 96	–		
12 months	.56*** n = 98	.65*** n = 87	–	
18 months	.39*** n = 91	.50*** n = 81	.55*** n = 86	–
24 months	.41** n = 86	.41* n = 75	.40*** n = 82	.46* n = 80

* $p < .05$, ** $p < .01$, *** $p < .001$.

based on CKD stage, the presence or absence of a hypertension diagnosis, or the number of prescribed antihypertensive medications at baseline (Table I).

Do Adherence, Self-Efficacy, Outcome Expectancies, and Barriers Change Over Time?

Adherence decreased linearly over time ($\beta = -2.98$, $SE = 0.69$, $t = -4.29$, $p < .001$); there was a significant random intercept for subject (variance estimate = 309.59, $SE = 65.26$, $Z = 4.74$, $p < .001$) but not a random slope. There was a quadratic effect for time,

with adherence exhibiting inverse curvilinear change over time ($\beta = -1.11$, $SE = 0.53$, $t = -2.09$, $p = .04$); there was a significant random intercept for subject (variance estimate = 315.06, $SE = 64.69$, $Z = 4.87$, $p < .001$) but not a random slope. Based on the AIC, the quadratic random intercept model (AIC = 4,404.20) was selected over the linear random intercept model (AIC = 4,409.10).

Self-efficacy did not change linearly over time ($\beta = 0.10$, $SE = 0.10$, $t = 0.96$, $p = .34$); there was a significant random intercept for subject (variance estimate = 1.11, $SE = 0.55$, $Z = 2.02$, $p = .02$) but not a random slope. Positive outcome expectancies did not change linearly over time ($\beta = -0.04$, $SE = 0.05$, $t = -0.75$, $p = .45$); the difference between the AIC was small for the random intercept model (AIC = 687.80) versus random intercept and slope model (AIC = 687.10). Therefore, the random intercept model was retained for modeling positive outcome expectancies over time, in which the random intercept for subject was not statistically significant. Negative outcome expectancies did not change linearly over time ($\beta = -0.04$, $SE = 0.05$, $t = -0.81$, $p = .42$); there was a significant random intercept for subject (variance estimate = 0.82, $SE = 0.16$, $Z = 5.11$, $p < .001$) but not a random slope. Barriers did not change linearly ($\beta = -0.07$, $SE = 0.04$, $t = -2.02$, $p = .05$); there was a significant random intercept for subject (variance estimate = 0.39, $SE = 0.07$, $Z = 5.88$, $p < .001$) and a random slope (variance estimate = 0.06, $SE = 0.03$, $Z = 2.03$, $p = .02$). There were no quadratic time effects in any of the models of health beliefs over time.

Are Self-Efficacy, Outcome Expectancies, Barriers, and Demographic Risk Factors Associated With Adherence Over Time?

In all models (Table V), adherence exhibited negative, curvilinear change over time; there were no main effects for adolescent age (baseline), gender, or race. Baseline family income was significantly associated with adherence over time in the self-efficacy, positive outcome expectancies, and barriers models but not the negative outcome expectancies model. Self-efficacy and positive and negative outcome expectancies (time varying) were significantly associated with adherence over time, but barriers (time varying) were not. None of the $\text{Time}^2 \times \text{predictor}$ interactions were statistically significant. There were significant random intercepts for subject in the positive and negative outcome expectancies models but not the self-efficacy or barriers models.

Discussion

Longitudinal, observational research is needed to clarify how medication adherence may change across

Table IV. Associations Between Self-Efficacy, Positive and Negative Outcome Expectancies, and Barriers Across 24 Months

	1	2	3	4	5	6	7	8	9	10	11
Baseline											
1. Self-efficacy	–										
2. Positive outcome expectancies	.50***	–									
3. Negative outcome expectancies	-.33***	-.14	–								
4. Barriers	-.44***	-.15	.71***	–							
12 months											
5. Self-efficacy	.48***	.27**	-.33**	-.31**	–						
6. Positive outcome expectancies	.32**	.54***	-.12	-.05	.61***	–					
7. Negative outcome expectancies	-.22*	-.17	.65***	.50***	-.45***	-.37***	–				
8. Barriers	-.24*	-.30**	.44***	.58***	-.26**	-.19	.63***	–			
24 months											
9. Self-efficacy	.40***	.28*	-.37***	-.38**	.65***	.51***	-.51***	-.39***	–		
10. Positive outcome expectancies	.23*	.45***	-.14	-.003	.45***	.72***	-.45***	-.22*	.57***	–	
11. Negative outcome expectancies	-.14	-.08	.66***	.51***	-.34**	-.28*	.80***	.58***	-.48***	-.43***	–
12. Barriers	-.16	-.14	.56***	.64***	-.34**	-.29*	.63***	.76***	-.51***	-.27*	.71***

Note. For correlations between baseline variables, $n = 112$ except for correlations with Barriers ($n = 105$). For correlations between baseline and 12-month variables, $n = 97$ except for correlations with Barriers ($n = 91$). For correlations between baseline and 24-month variables, $n = 84$ except for correlations with Barriers ($n = 78$). For correlations between 12-month variables, $n = 99$. For correlations between 12- and 24-month variables, $n = 83$. For correlations between 24-month variables, $n = 86$.

* $p < .05$, ** $p < .01$, *** $p < .001$.

adolescence and to identify potential treatment targets to improve long-term adherence. Demographic factors associated with greater risk for nonadherence should be considered in representative samples to illustrate the contexts in which adherence challenges may be most prominent. The current study addresses these issues in adolescents with CKD, a population for which there has been little empirical investigation of adherence despite known concerns with adherence (Blydt-Hansen et al., 2014) and clinical challenges with addressing it (Hashim et al., 2013). Results suggest that higher self-efficacy, positive beliefs about medications, and family income and fewer negative beliefs about medications are key predictors of higher antihypertensive adherence over 2 years in adolescents with CKD.

Consistent with evidence from other pediatric samples that adherence is a dynamic behavior (Modi et al., 2011; Smith et al., 2018), the current results demonstrated that antihypertensive medication adherence changed curvilinearly over time, with the lowest adherence observed 24 months after baseline. These data suggest that adherence likely fluctuates over the course of adolescence in the absence of intervention when clinically indicated and varies by individual. As adherence decreased, self-efficacy, positive and negative outcome expectancies, and barriers did not change over time. Therefore, adolescents with low self-efficacy and more negative and less positive beliefs

about their regimen will likely continue to experience these problems that also impact long-term adherence. The lack of longitudinal association between barriers and adherence highlights a likely lack of concordance between adolescents' perceived barriers and actual medication adherence.

As expected, older age, African American race, and lower SES (i.e., $\leq \$50,000$ family income, public health insurance) were associated with lower average adherence (i.e., the average of each adolescent's electronically monitored adherence across the five possible measurement points). However, female, rather than male, gender was associated with significantly lower average adherence. Given mixed findings on the association between gender and adherence (Naar-King et al., 2006; Quittner et al., 2014), relations between these variables may be sample dependent. Among adolescents in the current study, females may have had greater personal responsibility for managing their regimen than males, which has been observed in adolescents with other chronic illnesses including CKD (Javalkar et al., 2016). Assuming more independence for managing one's medical regimen in adolescence has been associated with poorer adherence (Modi, Marciel, Slater, Drotar, & Quittner, 2008). The potential role of gender differences on medication self-management warrants further investigation.

When the longitudinal influences of demographic risk factors on adherence were concurrently

Table V. Linear Mixed Models of Antihypertensive Medication Adherence Across 24 Months

Dependent variable for all models: Antihypertensive medication adherence									
Fixed effects	β	SE	<i>t</i>	<i>p</i>	Fixed effects	β	SE	<i>T</i>	<i>p</i>
Independent variable: Self-efficacy					Independent variable: Barriers to adherence				
Intercept	74.51	5.02	14.83	<.001	Intercept	75.05	5.28	14.21	<.001
Time	2.37	2.25	1.06	.29	Time	2.26	2.36	0.96	.34
Time ²	-1.35	0.55	-2.47	.01	Time ²	-1.30	0.57	-2.28	.02
Age	-1.10	0.76	-1.44	.15	Age	-0.91	0.79	-1.16	.25
Gender	-2.56	3.63	-.71	.48	Gender	-2.80	3.75	-0.75	.46
African American	-6.57	4.23	-1.55	.12	African American	-8.39	4.34	-1.93	.06
Other race	4.64	5.34	0.87	.39	Other race	5.54	5.57	0.99	.32
Income	10.77	4.17	2.58	.01	Income	10.94	4.43	2.47	.01
Self-efficacy	2.53	1.01	2.51	.01	Barriers	-4.74	2.63	-1.80	.07
Time ² × Self-efficacy	0.13	0.10	1.33	.19	Time ² × Barriers	.17	0.24	0.74	.46
Random effects	Variance estimate	SE	Z	<i>p</i>	Random effects	Variance Estimate	SE	Z	<i>p</i>
Intercept (individual)	139.27	106.88	1.30	.10	Intercept (individual)	135.49	118.14	1.15	.13
Independent variable: Positive outcome expectancies					Independent variable: Negative outcome expectancies				
Fixed effects	β	SE	<i>t</i>	<i>p</i>	Fixed effects	β	SE	<i>T</i>	<i>p</i>
Intercept	73.63	5.00	14.73	<.001	Intercept	77.18	5.17	14.94	<.001
Time	3.19	2.33	1.37	.17	Time	2.40	2.33	1.03	.31
Time ²	-1.50	0.57	-2.64	.01	Time ²	-1.35	0.57	-2.36	.02
Age	-1.01	0.76	-1.34	.18	Age	-1.14	0.77	-1.47	.14
Gender	-4.47	3.60	-1.24	.22	Gender	-3.04	3.68	-.83	.41
African American	-6.30	4.21	-1.50	.14	African American	-7.94	4.26	-1.86	.06
Other race	5.47	5.30	1.03	.30	Other	5.79	5.41	1.07	.29
Income	12.44	4.14	3.01	.003	Income	7.38	4.47	1.65	.10
Positive outcome expectancies	6.27	2.16	2.90	.004	Negative outcome expectancies	-4.13	1.72	-2.40	.02
Time ² × Positive outcome expectancies	0.04	0.22	0.17	.86	Time ² × Negative outcome expectancies	-.11	0.16	-.67	.50
Random effects	Variance estimate	SE	Z	<i>p</i>	Random effects	Variance Estimate	SE	Z	<i>p</i>
Intercept (individual)	158.18	87.37	1.81	.04	Intercept (individual)	184.28	82.32	2.24	.01

Note. For the categorical variables, female gender, Caucasian race, and $\geq \$50,000$ annual family income were the reference groups.

considered with self-efficacy, outcome expectancies, or barriers, family income was the only demographic factor that appeared to place adolescents with CKD at greater risk for lower adherence over time. This finding suggests that the context of living with financial stressors contributes to greater problems with adherence than age or identifying as a particular race or gender. Associations between lower financial resources and nonadherence have been reported frequently in the pediatric literature (Aylward et al., 2015; Modi et al., 2011). Among pediatric asthma patients, distinct barriers to adherence were identified for low-income families, including difficulty paying for prescription refills, endorsing negative beliefs about potential medication side effects, daily life hassles (e.g., paying bills and securing food) that interfere

with adherence, and distrusting recommendations given by medical providers (Bender & Bender, 2005). Adolescents with CKD from families with lower incomes may experience similar obstacles to adherence that uniquely impact adherence over time.

Self-efficacy and positive and negative outcome expectancies each predicted adherence over time, suggesting that positive beliefs in one's ability to adhere and favorable outcomes of adherence may offset the adverse impact of family income. Self-efficacy and outcome expectancies were time varying, suggesting that associations with adherence were consistent across the 24-month study and bidirectional. These findings may inform the development of adherence interventions that are consistent with the SCT framework for adolescents with CKD, which may delay

disease progression and the subsequent need for more intensive medical management. Such interventions may have potential to be adapted for adolescents with other diagnoses who take daily medications for similarly preventative reasons. Specifically, increasing self-efficacy and positive beliefs about medications may facilitate improvements in adherence. Negative beliefs about adherence outcomes may be amenable to change via cognitive restructuring (Beck, 2011) and low self-efficacy may be addressed through motivational interviewing techniques (Miller & Rollnick, 2013). Both treatment components have shown promise in improving adherence and disease control in adolescents with asthma (Riekert et al., 2011) and type 1 diabetes (Silverman, Hains, Davies, & Parton, 2003; Stanger et al., 2013). Multicomponent interventions that address cognitive, motivational, and behavioral factors may be the most successful approaches (Kahana et al., 2008).

This study had a number of strengths, including longitudinal data collected over 2 years with high retention rates, electronic medication monitoring, and a racially and socioeconomically diverse sample, but there were some limitations. The sample size was relatively small and the Other race category included adolescents who identified as Asian/Pacific Islander, multiracial, or other race; greater representation across racial backgrounds is needed in future research. Although 43% of adolescents approached for enrollment consented to join the study, we conducted universal screening of three separate pediatric nephrology clinics to actively recruit any adolescent identified as potentially eligible. There were no significant demographic differences found between those who participated versus those who declined to enroll, but it is possible that other sample characteristics contributed to the likelihood of joining this research study. Although the sample was recruited from multiple sites, the sites were, geographically, in the same region, and findings may not generalize to adolescents from other regions. Only antihypertensive medication was monitored during the study. Electronic monitoring, which was limited to 2 weeks per assessment period to reduce participant burden and support study retention, may be susceptible to reactivity effects (i.e., increased adherence because of the knowledge that one is being observed). Future researchers should consider monitoring adherence for a longer period of time, especially considering that the lowest adherence levels were at 24-month postbaseline, when adolescents may have habituated to using the MEMS cap.

High-quality observational findings, such as those reported in this study, should be translated into theoretically based, adherence-promoting interventions to test in clinical trials. The current findings suggest treatment approaches that contain motivational

interviewing and cognitive restructuring elements may support long-term antihypertensive medication adherence in adolescents with CKD. Although a small portion of pediatric psychologists reportedly uses these modalities when addressing nonadherence, the most frequently used treatment approach is problem solving (Wu et al., 2013). Further, other health-care providers with whom pediatric psychologists often collaborate to address patient nonadherence (e.g., physicians, nurses, and social workers) may not have received training or been exposed to psychologically based adherence-promoting strategies. Observational research on modifiable factors that impact adherence, as well as efficacious adherence interventions, should be disseminated not only to pediatric psychologists but also to interdisciplinary providers to broadly enhance the level of clinical care provided to adolescents with CKD and other adolescents who take daily medications.

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