

ORIGINAL RESEARCH

Implicit and Explicit Attitudes Toward Antihypertensive Medications Explain Variation in Pharmacy Refill and Self-Reported Adherence Beyond Traditional Risk Factors: Potential Novel Mechanism Underlying Adherence

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BACKGROUND: In pursuit of novel mechanisms underlying persistent low medication adherence rates, we assessed contributions of implicit and explicit attitudes, beyond traditional risk factors, in explaining variation in objective and subjective antihypertensive medication adherence.

METHODS AND RESULTS: Implicit and explicit attitudes were assessed using the difference scores from the computer-based Single Category Implicit Association Test and the *Necessity and Concerns* subscales of the Beliefs about Medicines Questionnaire, respectively. Antihypertensive medication adherence was measured using pharmacy refill proportion of days covered (PDC: mean PDC, low PDC <0.8) and the self-report 4-item Krousel-Wood Medication Adherence Scale (K-Wood-MAS-4: mean K-Wood-MAS-4, low adherence via K-Wood-MAS-4 ≥ 1). Hierarchical logistic and linear regression models controlled for traditional risk factors including social determinants of health, explicit, and implicit attitudes in a stepwise fashion. Community-dwelling insured participants ($n=85$: 44.7% female; 20.0% Black; mean age, 62.3 years; 43.5% low PDC, and 31.8% low adherence via K-Wood-MAS-4) had mean (SD) explicit and implicit attitude scores of 7.188 (5.683) and 0.035 (0.334), respectively. Low PDC was inversely associated with more positive explicit (adjusted odds ratio [aOR], 0.87; 95% CI, 0.78–0.98; $P=0.022$) and implicit (aOR, 0.12; 95% CI, 0.02–0.80; $P=0.029$) attitudes, which accounted for an additional 8.6% ($P=0.016$) and 6.5% ($P=0.029$) of variation in low PDC, respectively. Lower mean K-Wood-MAS-4 scores (better adherence) were associated only with more positive explicit attitudes (adjusted β , -0.04 ; 95% CI, -0.07 to -0.01 ; $P=0.026$); explicit attitudes explained an additional 5.6% ($P=0.023$) of K-Wood-MAS-4 variance.

CONCLUSIONS: Implicit and explicit attitudes explained significantly more variation in medication adherence beyond traditional risk factors, including social determinants of health, and should be explored as potential mechanisms underlying adherence behavior.

Key Words: 4-item Krousel-Wood Medication Adherence Scale ■ explicit attitudes ■ hypertension ■ implicit attitudes ■ proportion of days covered

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CLINICAL PERSPECTIVE

What Is New?

- Traditional risk factors including social determinants of health explained 20.8% of the variation in low pharmacy refill adherence (proportion of days covered <0.80); addition of implicit and explicit attitudes to the model (beyond the traditional risk factors) significantly increased the proportion of variation explained to 35.9%.
- Traditional risk factors including social determinants of health explained 22.8% of the variation in self-reported adherence (mean Krousel-Wood Medication Adherence Scale-4 item); addition of explicit attitudes to the model (beyond the traditional risk factors) significantly increased the proportion of variation explained to 28.4%, while inclusion of implicit attitudes did not explain additional variation.

What Are the Clinical Implications?

- Patient implicit and explicit attitudes toward antihypertensive medications may play important roles in medication-taking behavior, beyond traditional risk factors (including social determinants of health), in older adults with hypertension.
- Implicit attitudes toward medications may present additional targets for interventions to improve adherence to antihypertensive medications, which may improve blood pressure control and cardiovascular health.

Nonstandard Abbreviations and Acronyms

K-Wood-MAS-4	4-item Krousel-Wood Medication Adherence Scale
NIH	National Institutes of Health
PDC	proportion of days covered
SDOH	social determinants of health
SC-IAT	Single Category Implicit Association Test

Hypertension is a leading modifiable risk factor for premature death and disability, affecting more than 100 million women and men in the United States and over 1 billion people worldwide.^{1,2} Along with lifestyle modifications, pharmacological therapy is the cornerstone of treatment; most patients with hypertension require prescribed antihypertensive medication daily for the rest of their lives to control blood pressure, prevent adverse events, and improve healthy aging.³ However, full clinical benefit is dependent on patient initial (ie, “initiation”) and ongoing (ie,

“implementation”) adherence to prescribed therapy.⁴ Despite the well-established link between high medication adherence and good clinical outcomes, low adherence to medications persists as a clinical and public health challenge.⁵

To address this challenge, researchers have traditionally identified and targeted explicit patient, provider, and healthcare determinants of adherence behavior^{6–8} in interventions designed to improve medication taking. Yet only modest and short-term effects of these interventions on clinically meaningful outcomes have been demonstrated.^{9,10} Persistent low antihypertensive medication adherence rates^{11,12} suggest other patient-specific factors may be at play. Beyond more conscious or deliberative (ie, explicit) attitudes and motives for adhering to medications, research suggests that implicit attitudes may affect medication-taking behavior by acting as underlying subconscious or automatic, competing motives, that influence the actual taking of medications as prescribed.^{13,14} To that end, studies among patients with chronic psychiatric disorders¹⁵ and rheumatoid arthritis¹⁶ have suggested that medication adherence is driven by patient attitudes—both explicit and implicit—which may be associated with subjective and objective measures of adherence, respectively.^{15,16} In a more recent qualitative study of adults with hypertension, Herrera and colleagues showed that those who reported positive explicit attitudes toward medications had poor antihypertensive medication adherence, suggesting the presence of negative implicit attitudes working counter to participants’ expressed explicit attitudes.¹⁷ Despite these interesting findings, little is known about the role of implicit attitudes as an underlying mechanism and potential new target for medication adherence interventions in older adults with hypertension.

To aid identification of new targets for improving medication-taking behavior, the National Institutes of Health (NIH) Science of Behavior Change Initiative^{18,19} has recommended use of an experimental medicine approach to support rigor and efficacy in adherence intervention research. Specifically, the Science of Behavior Change methodology requires demonstration that mechanisms for behavior change are measurable, malleable, and causally linked to behavior.¹⁹ Therefore, we sought to expand on prior research, assess proof of concept, and demonstrate that implicit attitudes are measurable and associated with antihypertensive medication-taking behavior. Our primary objectives were to examine implicit (and explicit) attitudes in older adults with established and pharmacologically treated hypertension and determine their associations with validated objective and subjective medication adherence measures (ie, pharmacy refill adherence and the 4-item Krousel-Wood Medication Adherence Scale [K-Wood MAS-4], respectively). Results of this analysis

could inform planning of larger studies and provide important insights into potential new targets for interventions to improve medication adherence, and ultimately blood pressure control and quality of life, in adults with hypertension.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Sample

To demonstrate proof of concept, a minimum sample of 100 (achieved enrollment, N=106) insured, community-dwelling older adults, aged ≥55 years, was recruited from member lists of Blue Cross and Blue Shield of Louisiana (Blue Cross), a statewide health insurer and independent licensee of the Blue Cross and Blue Shield Association. Eligibility criteria included an *International Classification of Diseases, Clinical Modification, Ninth Revision (ICD-9-CM)* and *Tenth Revision (ICD-10-CM)* diagnosis of essential hypertension (from Blue Cross administrative databases and confirmed by self-report), current treatment with antihypertensive medication, and no moderate to severe cognitive impairment (defined as ≥3 errors on the brief cognitive 6-item screener).²⁰ Eligible participants completed a computer-based Single Category Implicit Association Test (SC-IAT)²¹ to measure their implicit attitudes toward medications. Following the SC-IAT, interviewer-administered questionnaires were used to obtain information including sociodemographic characteristics, other social determinants of health (SDOH), clinical history, medication adherence, and explicit attitudes toward antihypertensive medications. To obtain objective medication adherence information, data on pharmacy refills were extracted from Blue Cross administrative databases. The study was approved by the Tulane University Institutional Review Board. Written informed consent was obtained from all participants, and all study procedures were performed in accordance with institutional guidelines.

Study Measures

Predictor Variables

Implicit attitudes toward antihypertensive medications were measured with the computer-based SC-IAT using the Inquisit 4.0 software package (Millisecond Software, Seattle, WA).²² The SC-IAT is composed of 4 rounds of timed sorting tasks, namely, 2 test rounds of 72 trials (rounds B and D), each preceded by a practice round of 24 trials (rounds A and C), to aid understanding of the sorting task (Table 1). Rounds A and B paired images of taking antihypertensive pills with “good” words (eg, “happy”) for categorization using one computer response key while words reflecting “bad” attributes (eg, “awful”) were to be categorized using another response key. Rounds C and D switched the configuration so that only words reflecting “good” attributes (eg, “happy”) were to be categorized using the one response key, while images of individuals taking antihypertensive pills and words reflecting “bad” attributes (eg, “awful”) were to be categorized using the other response key. Participants were randomly assigned to 1 of 2 round orders: A-B-C-D or C-D-A-B. Any errors in categorization prompted on-screen notifications and required correction before proceeding.

Participants’ response times on each trial served as a proxy measure for implicit association strength, with faster response times indicative of stronger automatic associations. Only trials from test rounds were used to calculate individual SC-IAT difference scores (d-scores), defined as the mean response time on the trials pairing antihypertensive pills and a “bad” attribute (ie, test round D) minus the mean response time on the trials pairing antihypertensive pills and a “good” attribute (ie, test round B), divided by the SD of all response times within test rounds B and D. Higher scores indicated more positive implicit attitudes toward medication. For example, if a participant was faster at the task pairing images of persons taking antihypertensive medications with words reflecting “good” (versus “bad”) attributes, then this reflected relatively positive (versus negative) implicit attitudes toward antihypertensive medications. Good internal consistency and test-retest reliability has been demonstrated for SC-IAT tools.^{21,23} To ensure

Table 1. The Single Category Implicit Association Test (SC-IAT) Procedure*

Round	Trials	Function	Items Assigned to Left-Key Response	Items Assigned to Right-Key Response
A	24	Practice	Taking pills images+“Good” words	“Bad” words
B	72	Test	Taking pills images+“Good” words	“Bad” words
C	24	Practice	“Good” words	Taking pills images+“Bad” words
D	72	Test	“Good” words	Taking pills images+“Bad” words

*Participants were randomly assigned to one of two round orders: A-B-C-D or C-D-A-B. “Good” words included cheer, friend, glad, glee, happy, laugh, love, pleasure, smile, joy, glory, rejoice. “Bad” words included angry, destroy, dirty, dislike, evil, gross, nasty, pain, ugly, yucky, awful, fail.

high reliability, we adhered to specific procedures using at least 24 practice trials and 72 test trials, and excluding practice trials from the final calculation of SC-IAT scores.²¹

Explicit attitudes toward antihypertensive medications were evaluated using the specific version of the Beliefs About Medicines Questionnaire,^{6,24} consisting of two 5-item subscales, *Necessity* and *Concerns*, assessing positive and negative attitudes toward medication, respectively.⁶ Good internal consistency and test-retest reliability has been demonstrated for the Beliefs About Medicines Questionnaire measure.²⁴ Each item is assessed via a 5-point, Likert-type scale ranging from 1 (strongly agree) to 5 (strongly disagree). Scores for each item comprising the *Necessity* (Cronbach $\alpha=0.84$ in this study) and *Concerns* ($\alpha=0.77$ in this study) subscale were reverse-coded and summed. The relative importance of these explicit attitudes for participants, overall, was obtained by calculating the Necessity–Concerns differential, defined as the difference between *Necessity* and *Concerns* scores, with a possible range of -20 to 20 .⁶ A difference score of “0” indicated that an individual’s explicit attitudes toward antihypertensive medications were neutral. A positive difference score indicated that an individual’s necessity beliefs outweighed concerns about medications (ie, positive explicit attitude); a negative difference score indicated that concerns outweighed necessity beliefs (ie, negative explicit attitude).

Outcome Variables

Pharmacy refill adherence to antihypertensive medications was measured using the prescription-based proportion of days covered (PDC) for all antihypertensive prescriptions filled in the year before the survey.²⁵ PDC was calculated using fill dates and medication possession for all drugs within a given antihypertensive medication class as the number of days with medications available divided by the number of days between the first and last pharmacy fills.²⁵ The PDC for each antihypertensive medication class was calculated. An overall PDC was computed as the mean (possible range, 0–1) across all antihypertensive medication classes, with a higher score indicating better adherence. Low pharmacy refill adherence was defined using the commonly used cut point of PDC <0.80 ,^{25,26} which is associated with uncontrolled blood pressure and cardiovascular events.^{27,28}

Self-reported adherence to antihypertensive medications was assessed using the validated open-access K-Wood-MAS-4 tool. Developed to predict objective pharmacy refill adherence in older adults with established hypertension,²⁹ the K-Wood-MAS-4 reflects 4 aspects of adherence behavior: unintentional

nonadherence (ie, forgetfulness); intentional not taking of medications when one feels better; medication-taking self-efficacy; and physical functioning.^{28,29} Each response indicating suboptimal adherence, low self-efficacy, or health limitations is assigned 1 point. The K-Wood-MAS-4 score is calculated as the sum across the 4 response items (possible range, 0–4; higher scores reflecting worse adherence). Low adherence on the K-Wood-MAS-4 is defined as a score ≥ 1 based on moderate discrimination and optimal sensitivity and specificity using a cut point of ≥ 1 (C statistic=0.70, 95% CI, 0.68–0.71; sensitivity, 67.4%; specificity, 67.8%) as well as comparable performance to other validated self-reported measures.²⁹ In a prospective cohort of older adults, low adherence via K-Wood-MAS-4 (using a cut point of ≥ 1) was associated with uncontrolled blood pressure (adjusted odds ratio [aOR], 1.29; 95% CI, 1.01–1.65), incident cardiovascular events (adjusted hazard ratio, 2.29; 95% CI, 1.61–3.26),²⁸ and decline in mental health–related quality of life (aOR, 1.32; 95% CI, 1.08–1.62).³⁰

Covariates—Traditional Risk Factors

Key SDOH, including demographic, psychosocial, clinical, and healthcare system determinants³¹ of antihypertensive medication adherence were captured, according to published conceptual frameworks.^{32,33} Demographic characteristics included age (≥ 65 versus <65 years), sex (female versus male), race (Black versus White), marital status (married versus not married), and education (college education or higher versus less than college education); all participants were insured. Psychosocial factors included self-efficacy and depressive symptoms. Poor self-efficacy to manage hypertension was defined as mean score <9 on a 5-item validated measure of self-efficacy to manage disease (in this study, high blood pressure).³⁴ Depressive symptoms were measured using the validated 8-item Patient Health Questionnaire depression scale; depressive symptoms were defined using a standard cut point of ≥ 10 .³⁵ Clinical variables included the presence of obesity (defined as a body mass index, ≥ 30 kg/m²),³⁶ having been diagnosed with hypertension ≥ 10 years ago, presence of ≥ 2 comorbidities, and concurrent use of ≥ 4 other prescribed or over-the-counter medications as a surrogate for total medication burden. Healthcare system factors included trust in healthcare providers using the 11-item Trust in Physician Scale³⁷; mean scores were transformed to a 0 to 100 scale, with low trust defined as a score below the median.

Statistical Analysis

Descriptive statistics were computed to characterize the sample. Differences in mean implicit and explicit

attitude scores across participant characteristics were tested using Student *t* tests. Pearson correlation analyses were used to evaluate the strength and direction of associations between implicit and explicit attitudes.

To examine relationships between each attitude measure with low PDC adherence and low K-Wood-MAS-4 adherence, hierarchical *logistic* regression analyses were used. Model 1 contained traditional risk factors including SDOH, while Models 2 and 3 included explicit and implicit attitudes, respectively. Secondary analyses were also performed using multivariate, hierarchical *linear* regression analyses that modeled objective and self-reported adherence measures as continuous outcomes.^{38,39} For each outcome in the primary and secondary analyses, the proportion of variance explained by successive models was examined using the Nagelkerke's⁴⁰ R^2 and the R^2 generated in ordinary least squares regression, respectively. Nagelkerke's⁴⁰ R^2 was used based on its application in previous studies of implicit attitudes and adherence behaviors^{15,41} in addition to evidence from simulation studies that it provides a close approximation to R^2 values obtained in ordinary least squares regression.⁴² (Of note, Nagelkerke's R^2 is comparable across logistic regression models on low adherence [from the primary analysis] but should not be compared with R^2 s obtained from linear regression models on the overall adherence scores [the secondary analysis]). A continuous implicit-by-explicit interaction term was included in fully adjusted models for PDC and K-Wood-MAS-4 adherence. All analyses were performed using Stata v.15.1 software (StataCorp, College Station, TX).

RESULTS

Sample Characteristics

Analyses included the 85 (80.2%) participants with complete pharmacy refill data in the year before the survey. All 85 participants completed the computer-based SC-IAT. There were no statistically significant differences between those with complete (n=85) versus missing (n=21) pharmacy refill data with respect to age, sex, race, or education level. Those missing pharmacy refill data were less likely to be married than those with complete data ($P=0.007$).

Participants were 44.7% female, 20% Black (80.0% White), 73.8% married, average age of 62.3 years (SD, 4.9; range, 55–83 years), 54.1% had at least a college education (18% with high school education or less) (Table 2), and all were insured. All participants reported having a hypertension diagnosis for ≥ 1 years, with 83.5% and 63.5% having the diagnosis for at least 5 years and at least 10 years, respectively; 72.9% reported taking at least 4 prescribed

medications. Mean (SD) implicit attitudes score was 0.035 (0.334; range, -0.610 to 1.140). Mean (SD) explicit attitudes score was 7.188 (5.683; range, -4.000 to 20.000). Participants' implicit and explicit attitudes were not correlated ($r=0.07$; $P=0.533$). Mean implicit attitudes were similar across participant characteristics except for self-efficacy: Those with poor versus not poor self-efficacy had higher (more positive) mean implicit attitudes ($P=0.034$). For mean explicit attitudes, only those who were obese and who reported trust in their provider had higher (more positive) mean explicit attitudes toward their antihypertensive medications ($P<0.05$; Table 2).

Pharmacy Refill PDC Adherence Outcome

Among participants, 43.5% had low PDC (mean, 0.8; range, 0.1–1.0). Those with low versus not low PDC had mean implicit attitudes of -0.04 (range, -0.59 to 0.75 ; median, -0.09) versus 0.09 (range, -0.61 to 1.14 , respectively; median, 0.07) ($P=0.081$) and mean explicit attitudes of 5.86 (range, -4.00 to 20.00 ; median, 5.00) versus 8.21 (range, -1.00 to 20.00 , respectively; median, 7.50) ($P=0.059$) toward antihypertensive medications. In the fully adjusted primary analysis for PDC (model 3), more positive implicit attitudes and more positive explicit attitudes were associated with reduced odds of low PDC adherence (aOR, 0.12; 95% CI, 0.02–0.80; $P=0.029$; and aOR, 0.87; 95% CI, 0.78–0.98; $P=0.022$, respectively; Table 3). Other significant predictors of low PDC adherence included married status (aOR, 6.70; 95% CI, 1.60–28.11; $P=0.009$) and poor self-efficacy to manage hypertension (aOR=5.19, 95% CI 1.40, 19.25, $P=0.014$). The amount of variation in low PDC adherence explained in model 1 (traditional risk factors including SDOH) was 20.8%; in model 2 (adding explicit attitudes), this increased to 29.4% (8.6% increase over model 1; $\chi^2=5.76$; $P=0.016$), and in model 3 (adding implicit attitudes) to 35.9% (6.5% increase over model 2; $\chi^2=4.80$; $P=0.029$). No significant predictors emerged in secondary analyses modeling pharmacy refill PDC adherence as a continuous outcome. There was no interaction effect of implicit and explicit attitudes on PDC adherence in either the primary or secondary analysis ($P>0.05$; Table 3).

Self-Reported K-Wood-MAS-4 Adherence Outcome

Among participants, 31.8% reported low adherence via K-Wood-MAS-4 (mean, 0.5; range, 0–3). Mean implicit and explicit attitudes between those with low versus not low adherence via K-Wood-MAS-4 were as follows: mean implicit attitudes of 0.01 (range, -0.61 to 1.14 ; median, -0.07) versus 0.04 (range, -0.59 to 0.75 ; median 0.03), respectively ($P=0.709$), and mean explicit attitudes of 6.74

Table 2. Participant Characteristics: Overall and by Implicit and Explicit Attitudes (N=85)

	Overall		Implicit Attitudes			Explicit Attitudes		
	N	%	Mean	SD	P Value	Mean	SD	P Value
Sociodemographic								
Age-group								
Aged <65 y	65	76.47	0.036	0.360	0.942	7.277	5.965	0.797
Aged ≥65 y	20	23.53	0.030	0.238		6.900	4.778	
Sex								
Male	47	55.29	0.079	0.347	0.177	7.085	5.614	0.854
Female	38	44.71	-0.020	0.313		7.316	5.841	
Race								
White	68	80.00	0.010	0.330	0.177	7.059	5.192	0.677
Black	17	20.00	0.133	0.341		7.706	7.506	
Marital status								
Not married	22	26.19	0.035	0.378	0.997	7.091	5.424	0.871
Married	62	73.81	0.035	0.323		7.323	5.805	
Education level								
Less than college education	39	45.88	0.080	0.360	0.256	7.410	5.959	0.742
College education or greater	46	54.12	-0.003	0.308		7.000	5.497	
Psychosocial								
Poor self-efficacy to manage hypertension								
No	36	42.35	-0.054	0.335	0.034	8.000	5.831	0.262
Yes	49	57.65	0.100	0.321		6.592	5.556	
Depressive symptoms								
No	76	90.48	0.024	0.316	0.476	7.553	5.827	0.095
Yes	8	9.52	0.114	0.507		4.000	3.162	
Clinical								
Obesity								
No (BMI <30 kg/m ²)	45	52.94	0.003	0.331	0.359	5.911	4.542	0.027
Yes (BMI ≥30 kg/m ²)	40	47.06	0.070	0.338		8.625	6.503	
Hypertension duration ≥10 y								
No	31	36.47	0.046	0.323	0.815	6.355	6.275	0.309
Yes	54	63.53	0.028	0.343		7.667	5.316	
≥2 comorbidities								
No	81	95.29	0.041	0.335	0.465	7.247	5.423	0.671
Yes	4	4.71	-0.085	0.336		6.000	10.863	
Taking ≥4 medications								
No	23	27.06	-0.068	0.261	0.083	5.870	4.827	0.194
Yes	62	72.94	0.073	0.351		7.677	5.931	
Healthcare system								
Low trust in provider								
No	40	47.06	0.047	0.336	0.763	9.600	6.201	<0.001
Yes	45	52.94	0.024	0.335		5.044	4.194	

Two participants missing observations (married status: n=1; depressive symptoms: n=1). *P*-values based on Student *t* test. Implicit and explicit attitudes are based on difference scores from the Single Category Implicit Association Test and the Beliefs about Medicines Questionnaire *Necessity* and *Concerns* subscales, respectively, with higher scores indicative of more positive attitudes. BMI indicates body mass index.

(range, -4.00 to 20.00; median, 6.00) versus 7.40 (range -4.00 to 20.00, respectively; median: 7.00), respectively (*P*=0.623). In the fully adjusted primary analysis (model 3), female sex (aOR, 4.00; 95% CI,

1.18–13.64; *P*=0.027) and obese status (aOR, 3.83; 95% CI, 1.07–13.72; *P*=0.039; Table 4) were significantly associated with low adherence via K-Wood-MAS-4. The amount of variation in low adherence via

Table 3. Multivariate, Hierarchical Regression Models Predicting Pharmacy Refill Proportion of Days Covered (PDC) Adherence (N=85)

	Primary Analysis (Categorical Outcome) Logistic Regression on Low PDC adherence			Secondary Analysis (Continuous Outcome) Linear Regression on Overall PDC Adherence Score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3*
	OR (95% CI)	OR (95% CI)	OR (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sociodemographic						
Age group						
Aged <65 y	REF	REF	REF	REF	REF	REF
Aged ≥65 y	1.08 (0.32 to 3.61)	1.07 (0.30 to 3.79)	1.35 (0.35 to 5.18)	-0.02 (-0.16 to 0.12)	-0.02 (-0.15 to 0.12)	-0.02 (-0.16 to 0.11)
Sex						
Male	REF	REF	REF	REF	REF	REF
Female	1.01 (0.36 to 2.82)	1.22 (0.41 to 3.61)	0.91 (0.29 to 2.89)	-0.02 (-0.14 to 0.10)	-0.03 (-0.14 to 0.09)	-0.01 (-0.13 to 0.11)
Race						
White	REF	REF	REF	REF	REF	REF
Black	1.27 (0.34 to 4.82)	1.40 (0.32 to 6.05)	2.08 (0.43 to 10.14)	-0.02 (-0.18 to 0.13)	-0.03 (-0.18 to 0.12)	-0.06 (-0.21 to 0.09)
Marital status						
Not married	REF	REF	REF	REF	REF	REF
Married	4.97 (1.35 to 18.32) [†]	7.21 (1.73 to 30.17) [‡]	6.70 (1.60 to 28.11) [‡]	-0.12 (-0.24 to 0.01)	-0.13 (-0.26 to 0.00) [†]	-0.12 (-0.25 to 0.00)
Education level						
Less than college education	REF	REF	REF	REF	REF	REF
College education or greater	0.68 (0.24 to 1.92)	0.79 (0.27 to 2.38)	0.69 (0.22 to 2.21)	0.01 (-0.11 to 0.13)	-0.01 (-0.13 to 0.11)	0.00 (-0.11 to 0.12)
Psychosocial						
Poor self-efficacy to manage hypertension						
No	REF	REF	REF	REF	REF	REF
Yes	3.69 (1.14 to 11.90) [†]	3.66 (1.05 to 12.79) [†]	5.19 (1.40 to 19.25) [†]	-0.11 (-0.23 to 0.01)	-0.10 (-0.22 to 0.02)	-0.12 (-0.24 to 0.00)
Depressive symptoms						
No	REF	REF	REF	REF	REF	REF
Yes	0.37 (0.07 to 2.08)	0.22 (0.03 to 1.33)	0.21 (0.03 to 1.50)	0.06 (-0.15 to 0.26)	0.10 (-0.11 to 0.30)	0.08 (-0.12 to 0.29)
Clinical						
Obese (BMI ≥30 kg/m ²)						
No	REF	REF	REF	REF	REF	REF
Yes	1.39 (0.48 to 4.04)	2.19 (0.67 to 7.17)	2.64 (0.74 to 9.37)	-0.04 (-0.16 to 0.09)	-0.08 (-0.20 to 0.05)	-0.08 (-0.20 to 0.05)
Hypertension duration ≥10 y						
No	REF	REF	REF	REF	REF	REF
Yes	1.35 (0.47 to 3.87)	1.55 (0.51 to 4.68)	1.34 (0.43 to 4.14)	0.04 (-0.08 to 0.16)	0.03 (-0.09 to 0.14)	0.03 (-0.08 to 0.15)
≥2 comorbidities						
No	REF	REF	REF	REF	REF	REF
Yes	1.00 (0.09 to 11.35)	0.64 (0.05 to 8.40)	0.30 (0.02 to 5.08)	0.07 (-0.23 to 0.36)	0.11 (-0.18 to 0.39)	0.15 (-0.14 to 0.45)
Taking ≥4 medications						
No	REF	REF	REF	REF	REF	REF
Yes	0.32 (0.09 to 1.11)	0.35 (0.09 to 1.28)	0.41 (0.11 to 1.50)	0.08 (-0.05 to 0.22)	0.06 (-0.07 to 0.20)	0.06 (-0.08 to 0.19)

(Continued)

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Table 3. Continued

	Primary Analysis (Categorical Outcome) Logistic Regression on Low PDC adherence			Secondary Analysis (Continuous Outcome) Linear Regression on Overall PDC Adherence Score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3*
	OR (95% CI)	OR (95% CI)	OR (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Healthcare system						
Low trust in provider						
No	REF	REF	REF	REF	REF	REF
Yes	1.25 (0.47 to 3.36)	0.69 (0.22 to 2.14)	0.70 (0.21 to 2.30)	-0.01 (-0.12 to 0.10)	0.04 (-0.08 to 0.17)	0.04 (-0.08 to 0.16)
Explicit attitudes		0.87 (0.78 to 0.98) [†]	0.87 (0.78 to 0.98) [†]		0.01 (0.00 to 0.02) [†]	0.01 (0.00 to 0.02)
Implicit attitudes (d-score)			0.12 (0.02 to 0.80) [†]			0.13 (-0.04 to 0.31)
R ²	0.208	0.294	0.359	0.106	0.158	0.187
ΔR^2		0.086	0.065		0.052	0.028
Wald test	10.08	5.76 [†]	4.80 [†]	0.69	4.26 [†]	2.36

Two participants missing observations (married status: n=1; depressive symptoms: n=1). Implicit and explicit attitudes are based on difference scores from the Single Category Implicit Association Test and the Beliefs about Medicines Questionnaire *Necessity* and *Concerns* subscales, respectively, with higher scores indicative of more positive attitudes. BMI indicates body mass index; and OR, odds ratio.

*There was no interaction effect of implicit and explicit attitudes on PDC adherence (primary analysis: OR, 0.80; 95% CI, 0.56 to 1.15, *P*-interaction=0.230; and secondary analysis: β =0.003; 95% CI, -0.03 to 0.04; *P*-interaction=0.875).

[†]*P*<0.05.

[‡]*P*<0.01.

K-Wood-MAS-4 explained in model 1 (traditional risk factors including SDOH) was 22.7%. In model 2 (adding explicit attitudes), this increased to 24.4% (1.7% increase over model 1; $\chi^2=1.13$; *P*>0.05); there was no increase with the addition of implicit attitudes (model 3: 0% increase over model 2; $\chi^2=0.06$; *P*>0.05). In the fully adjusted secondary analysis modeling K-Wood-MAS-4 adherence as a continuous outcome (model 3), only more positive explicit attitudes toward antihypertensive medications were associated with lower (better) adherence scores (adjusted $\beta=-0.04$, 95% CI -0.07, 0.00, *P*=0.026). Implicit attitudes were not associated with K-Wood-MAS-4 adherence (adjusted β , -0.05; 95% CI, -0.57 to 0.47; *P*=0.843). The amount of variation in mean K-Wood-MAS-4 adherence explained in model 1 (traditional risk factors including SDOH) was 22.8%. In model 2 (adding explicit attitudes), this increased to 28.4% (5.6% increase over model 1; *F*=5.37; *P*=0.023); there was no increase in model 3 (adding implicit attitudes) (*R*²=28.4%; *F*=0.04; *P*>0.05). There was no interaction effect of implicit and explicit attitudes on self-reported K-Wood-MAS-4 adherence in either the primary or secondary analysis (*P*>0.05; Table 4).

DISCUSSION

While it is established that antihypertensive medication adherence behavior is multifactorial,^{32,33} to our knowledge, the added value of implicit *and* explicit attitudes, over traditional risk factors including SDOH, in

explaining both objective (ie, PDC) *and* self-reported (ie, K-Wood-MAS-4) antihypertensive medication adherence, among older adults, has not been previously reported. In fully adjusted models, both implicit and explicit attitudes were associated with pharmacy refill adherence. Beyond traditional risk factors, explicit attitudes accounted for an additional 8.6% of the variation in low PDC adherence with implicit attitudes explaining a further 6.5% of the variance in low PDC adherence. Furthermore, explicit, but not implicit, attitudes were associated with self-reported adherence, with explicit attitudes explaining an additional 5.6% of the variance in the self-reported K-Wood-MAS-4 adherence mean score (beyond traditional risk factors), while implicit attitudes did not contribute to the variation in the outcome explained.

In this proof-of-concept study, our findings are consistent with prior studies in patients with other chronic diseases, where implicit and explicit attitudes were uncorrelated and marginal associations between explicit, but not implicit, attitudes and self-reported adherence were observed.^{15,16} Collectively, these results suggest that implicit and explicit attitudes influence different behaviors along the medication-taking cascade. Implicit attitudes toward medications may explain a unique aspect of medication adherence that is not explained by self-reported explicit attitudes and may not be associated with self-reported adherence. These findings reinforce the utility of employing objective and subjective adherence measures in medication adherence research and

Table 4. Multivariate, Hierarchical Regression Models Predicting Self-Reported Krousel-Wood Medication Adherence Scale-4-item (K-Wood-MAS-4) Adherence (N=85)

	Primary Analysis (Categorical Outcome) Logistic Regression on Low K-Wood-MAS-4 Adherence			Secondary Analysis (Continuous Outcome) Linear Regression on Overall K-Wood-MAS-4 Adherence Score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3*
	OR (95% CI)	OR (95% CI)	OR (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sociodemographic						
Age group						
Aged <65 y	REF	REF	REF	REF	REF	REF
Aged ≥65 y	1.43 (0.36 to 5.65)	1.39 (0.35 to 5.56)	1.41 (0.35 to 5.63)	0.08 (−0.33 to 0.49)	0.07 (−0.33 to 0.46)	0.07 (−0.33 to 0.47)
Sex						
Male	REF	REF	REF	REF	REF	REF
Female	3.90 (1.22 to 12.45) [†]	4.18 (1.29 to 13.58) [†]	4.00 (1.18, 13.64) [†]	0.20 (−0.14 to 0.55)	0.23 (−0.11 to 0.57)	0.22 (−0.13 to 0.57)
Race						
White	REF	REF	REF	REF	REF	REF
Black	2.31 (0.62 to 8.68)	2.35 (0.62 to 8.88)	2.44 (0.62 to 9.61)	0.26 (−0.20 to 0.71)	0.27 (−0.17 to 0.71)	0.28 (−0.17 to 0.74)
Marital status						
Not married	REF	REF	REF	REF	REF	REF
Married	1.25 (0.35 to 4.39)	1.38 (0.38 to 4.99)	1.36 (0.37 to 4.94)	0.06 (−0.33 to 0.44)	0.11 (−0.26 to 0.49)	0.11 (−0.27 to 0.49)
Education level						
Less than college education	REF	REF	REF	REF	REF	REF
College education or greater	1.14 (0.38 to 3.45)	1.24 (0.40 to 3.80)	1.22 (0.39 to 3.78)	−0.10 (−0.45 to 0.25)	−0.03 (−0.38 to 0.32)	−0.03 (−0.39 to 0.32)
Psychosocial						
Poor self-efficacy to manage hypertension						
No	REF	REF	REF	REF	REF	REF
Yes	0.55 (0.17 to 1.83)	0.50 (0.15 to 1.73)	0.52 (0.15 to 1.87)	−0.18 (−0.54 to 0.18)	−0.24 (−0.59 to 0.12)	−0.23 (−0.60 to 0.14)
Depressive symptoms						
No	REF	REF	REF	REF	REF	REF
Yes	3.53 (0.59 to 21.01)	2.78 (0.45 to 17.40)	2.80 (0.44 to 17.68)	0.62 (0.01 to 1.23) [†]	0.48 (−0.12 to 1.09)	0.49 (−0.12 to 1.10)
Clinical						
Obese (BMI ≥30 kg/m ²)						
No	REF	REF	REF	REF	REF	REF
Yes	3.12 (0.94 to 10.40)	3.82 (1.07 to 13.64) [†]	3.83 (1.07 to 13.72) [†]	0.21 (−0.16 to 0.57)	0.33 (−0.04 to 0.70)	0.33 (−0.04 to 0.71)
Hypertension duration ≥10 y						
No	REF	REF	REF	REF	REF	REF
Yes	1.24 (0.40 to 3.88)	1.32 (0.42 to 4.20)	1.30 (0.41 to 4.17)	0.12 (−0.23 to 0.47)	0.16 (−0.18 to 0.50)	0.16 (−0.19 to 0.50)
≥2 comorbidities						
No	REF	REF	REF	REF	REF	REF
Yes	1.41 (0.12 to 16.00)	1.19 (0.09 to 15.19)	1.11 (0.08 to 15.22)	0.91 (0.04 to 1.78) [†]	0.78 (−0.07 to 1.63)	0.76 (−0.12 to 1.63)

(Continued)

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Table 4. Continued

	Primary Analysis (Categorical Outcome) Logistic Regression on Low K-Wood-MAS-4 Adherence			Secondary Analysis (Continuous Outcome) Linear Regression on Overall K-Wood-MAS-4 Adherence Score		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3*
	OR (95% CI)	OR (95% CI)	OR (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Taking ≥4 medications						
No	REF	REF	REF	REF	REF	REF
Yes	1.77 (0.43 to 7.26)	2.02 (0.47 to 8.62)	2.01 (0.47 to 8.55)	0.04 (−0.36 to 0.44)	0.10 (−0.29 to 0.49)	0.10 (−0.30 to 0.50)
Healthcare system						
Low trust in provider						
No	REF	REF	REF	REF	REF	REF
Yes	1.34 (0.46 to 3.86)	1.01 (0.31 to 3.28)	1.02 (0.31 to 3.33)	0.12 (−0.22 to 0.45)	−0.06 (−0.41 to 0.30)	−0.06 (−0.42 to 0.30)
Explicit attitudes		0.94 (0.85 to 1.05)	0.94 (0.85 to 1.05)		−0.04 (−0.07 to −0.01) [†]	−0.04 (−0.07 to 0.00) [†]
Implicit attitudes (d-score)			0.81 (0.14 to 4.54)			−0.05 (−0.57 to 0.47)
R ²	0.227	0.244	0.244	0.228	0.284	0.284
ΔR ²		0.017	0.000		0.056	0.000
Wald test	11.13	1.13	0.06	1.72	5.37 [†]	0.04

Two participants missing observations (married status n=1; depressive symptoms n=1). Implicit and explicit attitudes are based on difference scores from the Single Category Implicit Association Test and the Beliefs About Medicines Questionnaire *Necessity* and *Concerns* subscales, respectively, with higher scores indicative of more positive attitudes. BMI indicates body mass index; and OR, odds ratio.

*There was no interaction effect of implicit and explicit attitudes on self-reported K-Wood-MAS-4 adherence (primary analysis: OR, 1.11; 95% CI, 0.81 to 1.51, *P*-interaction=0.516; and secondary analysis: β=0.01, 95% CI −0.09 to 0.11; *P*-interaction=0.792).

[†]*P*<0.05.

clinical practice.^{43,44} Objective pharmacy refill measures of adherence may be needed to understand the relationship between subconscious attitudes and adherence behavior and to assess the impact of interventions focusing on improving implicit attitudes toward medications as the underlying mechanism. Meanwhile, self-reported adherence measures like the K-Wood-MAS-4 identify explicit reasons for nonadherence (eg, intentionally not taking medications) and provide important insight into mechanisms linking explicit attitudes to various aspects of medication-taking behavior.

Attitudes are shaped by deliberative/conscious and automatic/subconscious processes.^{14,45} According to Wilson et al,¹⁴ implicit attitudes guide behavior that people do not monitor consciously, while explicit attitudes predict behavior that is more conscious (ie, planned). Thus, when patients are asked to evaluate deliberately and report how positive they are about a medication, they are tapping into their explicit, conscious attitudes. These self-reports are restricted to the limits of awareness and susceptible to response bias. In contrast to explicit attitudes, implicit attitudes—as measured using reaction-time tasks such as the SC-IAT²¹—are automatically activated, can occur outside of the individual’s conscious awareness and control,

and may predict adherence behavior more accurately than explicit attitudes, particularly among people with established disease.^{16,46}

In our prior work with a sample of patients taking chronic disease medications, we used psychological interviews to explore behavior goals (eg, to take medications as prescribed), behaviors that work against those goals (eg, skipping doses), subconscious commitments that compete with the behavior goal (eg, not wanting to be overwhelmed with daily drug schedule), and the assumptions or negative implicit attitudes underlying those subconscious commitments (eg, if I take medicines, I will be stressed).¹³ A patient might believe that medications improve blood pressure control and report positivity about taking medications (positive explicit attitudes). However, the actual *taking of medication* reminds the patient that he or she feels stressed about needing to remember the drug schedule (negative implicit attitudes) leading to subconscious resistance to adhere. Taken together with findings from this study, these data underscore the need for both objective and self-reported adherence measures, support the role of automatic/subconscious processes underlying medication nonadherence in older adults, and position medication taking as an adaptive challenge, requiring

changes in one's mind set to address implicit attitudes and achieve adherence goals.

In addition to implicit and explicit attitudes, low PDC adherence was associated with poor self-efficacy to manage hypertension and married status. Associations between increased self-efficacy and better adherence are well described.⁴⁷ Previous studies have reported a protective effect of marriage on medication adherence for elderly males, noting that marital quality likely influences this relationship.⁴⁸ Further investigation is needed to understand the association between marital status and poor refill adherence. Consistent with the literature, female sex and obese status were positively associated with low self-reported adherence via K-Wood-MAS-4.^{49,50}

Results should be interpreted considering study limitations. While our sample included 20% Black participants and 18% with a high school education or less, this study sample of older insured adults from one region of the United States was largely White and married, with about half reporting a college-level education; thus, the results may not be generalizable to all people with hypertension. We acknowledge that this study may not be adequately powered to detect differences across age, sex, and race. Additional research in larger, more racially, geographically, and socially diverse samples is needed to confirm these findings. Larger studies should be conducted to further examine this issue and to explore differences by sex and race. The adherence tools used are indirect measures of adherence. Although we were able to account for several key social and other determinants of health influencing antihypertensive medication adherence (eg, demographics, self-efficacy, trust in healthcare provider, presence of comorbidities),^{12,32,48–50} the analysis did not account for all SDOH (eg, income, health literacy). Future work should also consider total medication complexity and attitudes toward total medication burden. Finally, this was a cross-sectional analysis and causal inferences regarding the impact of implicit or explicit attitudes on medication-taking behavior cannot be made.

There are several strengths of the study, including use of multiple, validated tools to measure attitudes and adherence behavior. In addition, these results advance the field by examining relationships between implicit *and* explicit attitudes with antihypertensive medication-taking behavior, beyond traditional risk factors including key SDOH, comorbidity and total medication burden, using both objective (ie, PDC) *and* self-reported (ie, K-Wood-MAS-4) measures of adherence. We modeled the outcomes as both categorical and continuous variables (ie, primary versus secondary analyses) and propose that linear treatment of the 4-item K-Wood-MAS-4 scale may have enabled greater power to detect significant

associations,⁵¹ while evidence of clinical benefit only at, or above, a threshold of 0.80⁵² may justify categorization of PDC adherence into homogenous groups reflecting “low” and “not low” adherers. In keeping with the NIH Science of Behavior Change approach described earlier, our study's findings that implicit attitudes toward antihypertensive medications can be measured and that such attitudes are associated with objective measures of adherence suggest that implicit attitudes may be a novel mechanism underlying adherence behavior and may constitute a potential new target for adherence research aimed at improving medication-taking behavior in older adults with hypertension.

Future research in larger, more diverse populations, demonstrating that implicit attitudes are malleable and that improvement in implicit attitudes is causally associated with better adherence that translates into improved health outcomes would align with the Science of Behavior Change experimental medicine framework and inform targeted interventions to promote adherence and blood pressure control. Recent work has demonstrated that while attitudes are generally stable over time, explicit and implicit attitudes are susceptible to change with intervention⁵³; in particular, behavior change strategies involving cognitive-behavioral therapy and motivational interviewing techniques have shown promise in changing implicit attitudes.⁵⁴ Additional research is underway using longitudinal and clinical trial designs to examine whether interventions targeting positive changes in implicit attitudes result in improvements in medication-taking behavior and ultimately blood pressure control.

CONCLUSIONS

Patient implicit and explicit attitudes toward medications may play important roles in medication-taking behavior, beyond traditional risk factors including key SDOH, in older adults with hypertension. The differential association of implicit and explicit attitudes with objective and self-reported measures of adherence may reflect the unique roles of automatic/subconscious and deliberative/conscious attitudes in guiding distinct behaviors across the medication-taking cascade. Furthermore, implicit attitudes toward medications may underlie adherence behavior and serve as a novel target for interventions designed to achieve clinically meaningful medication-taking behavior change in older adults with hypertension and low adherence. Based on the results of this study demonstrating proof of concept, further research into the clinical utility of SC-IAT in assessing implicit attitudes about medications and the efficacy of interventions targeting improvement

in implicit attitudes as the potential mechanism underlying change in medication-taking behavior is underway.

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Disclosures

None.

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