Race-Ethnic Differences in Factors Associated with Inhaled Steroid Adherence among Adults with Asthma

Karen Wells¹, Manel Pladevall², Edward L. Peterson¹, Janis Campbell², Mingqun Wang², David E. Lanfear^{2,3}, and L. Keoki Williams^{1,2,3}

¹Department of Biostatistics and Research Epidemiology, ²Center for Health Services Research, and ³Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan

Rationale: Adherence to inhaled corticosteroid (ICS) medication is known to be low overall, but tends to be lower among African-American patients when compared with white patients.

Objectives: To understand the factors that contribute to ICS adherence among African-American and white adults with asthma.

Methods: Eligible individuals had a prior diagnosis of asthma, one or more ICS prescriptions, and were members of a large health maintenance organization in southeast Michigan. Individuals were sent a survey that included questions about internal factors (e.g., patient beliefs, knowledge, and motivation) and external factors (e.g., socioeconomic status, barriers to care, social support, and stressors) potentially related to ICS adherence. Adherence was calculated using electronic prescription and fill data. Stepwise regression was used to identify factors associated with adherence before and after stratifying by race-ethnicity.

Measurements and Main Results: Surveys were returned by 1,006 (56.3%) of 1,787 eligible patients. Adjusting for internal factors, but not external factors, diminished the relationship between race-ethnicity and ICS adherence. Among African-American patients, readiness to take ICS medication was the only internal or external factor significantly associated with ICS adherence; it explained 5.6% of the variance in adherence. Among white patients, perceived ICS necessity, ICS knowledge, doctors being perceived as the source of asthma control, and readiness to take medication were the internal factors associated with ICS adherence; these accounted for 19.8% of the variance in adherence.

Conclusions: Factors associated with ICS adherence appear to differ between African-American and white patients, suggesting that group-specific approaches are needed to improve adherence.

Keywords: medication adherence; inhaled corticosteroids; asthma; race-ethnicity; patient compliance

Inhaled corticosteroid (ICS) medication is the most consistently effective long-term control therapy for persistent asthma, yet patient adherence to ICS treatment is low (1–4). Poor adherence to ICS medication is associated with increased asthma-related emergency department visits and hospitalizations and an increased need for oral corticosteroids (1, 4).

Differences in medication adherence by race-ethnicity exist and have been noted in several studies (2, 5–8). This may be the result of external factors, such as income, possession of commercial health insurance (5), psychosocial stressors (e.g., resi-

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Differences in inhaled corticosteroid (ICS) adherence by race-ethnicity is well described, and may account for disparities in asthma-related outcomes. However, less well known are the factors associated with medication adherence within these groups.

What This Study Adds to the Field

Here we show that the factors associated with ICS adherence appear to differ between African-American and white patients. This suggests that differing approaches may be needed to improve adherence among these race-ethnic groups and future interventions tailored accordingly.

dential crime rates) (2, 9), and characteristics of the facility where care is provided (6).

In addition, internal factors, such as patients' beliefs, knowledge, and motivation, may also influence adherence to asthma therapy. These include but are not limited to patient perceptions about the necessity of treatment (10), concerns surrounding medication use (11), perceived control over one's health (12, 13), and readiness take medications as prescribed (14).

While internal and external factors may not be completely independent, this dichotomization provides a useful framework for assessing many of the behavioral and environmental factors reportedly associated with medication adherence. Using claims-based metrics of medication use, we assessed the factors associated with ICS adherence in a large patient population. The size and diversity of this patient population allowed us to also assess differences in these factors by race-ethnicity.

METHODS

Study Population and Setting

This study was approved by the Institutional Review Board at Henry Ford Health System and was in compliance with its Health Insurance Portability and Accountability Act policy. Patients were both members of a large health maintenance organization (HMO) in southeast Michigan, and they received their care from a large, multispecialty medical group. These patients were also participants in a cluster-randomized trial to improve adherence to ICS medication (ClinicalTrials.gov number NCT00459368). The data used in this analysis represent the baseline measures collected as part of this trial, including responses to the pre-intervention survey. Unlike the trial that included patients aged 5 to 56 years, we restricted this analysis to patients aged 18 years or older to understand the factors contributing to nonadherence in adults. Patients also met the following criteria: at least one electronic prescription for an ICS before April 30, 2007; continuous enrollment in the HMO for the 12 months before the date of the first electronic ICS prescription (i.e., the index date); at least one clinical diagnosis of asthma and no

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Correspondence and requests for reprints should be addressed to L. Keoki Williams, M.D., M.P.H., Center for Health Services Research, Henry Ford Hospital, 1 Ford Place, 3A CHSR, Detroit, MI 48202. E-mail: kwillia5@hfhs.org

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diagnoses of chronic obstructive pulmonary disease or congestive heart failure in the 12 months before the index date; and an index ICS prescription with at least one refill prescribed. The last criterion was included to ensure that the patient was supposed to be on continuous ICS therapy, an implicit assumption in claims-based measures of adherence. We have also previously shown that a clinical diagnosis of asthma in our data systems is highly predictive of patient-reported asthma (15). We excluded patients whose last ICS prescription was explicitly stopped by their physician.

Calculating ICS Adherence

Adherence was calculated in a manner similar to that in our previous studies, using automated data from electronic prescriptions (DrFirst Inc., Rockville, MD) and pharmacy claims (3). Briefly, we linked electronic prescription information with fill information from pharmacy claims data to estimate the number of days that a given fill of an ICS would last (i.e., days supplied). This was calculated by dividing the canister size (i.e., puffs per canister) as derived from National Drug Codes in pharmacy claims by the dosage information (i.e., puffs per day). The calculated days' supply was then used to estimate a continuous measure of medication adherence, otherwise known as a continuous, multiple-interval measure of medication availability (CMA) (16), where $CMA = \text{Cumulative days' supplied} / \text{Number of days of observation}$. This can be interpreted as the proportion of time that the patient had medication available. We calculated adherence for a 6-month period of observation beginning November 21, 2006 and ending May 21, 2007. To account for potential medication surplus leading into the period of observation, we accounted for all fills 3 months before its start. Although these metrics may underestimate adherence if patients fill medications through other insurance coverage (e.g., that provided by a parent or spouse), we have previously shown that this occurs rarely (< 1% of patients) in this patient population (3). The time interval for measuring adherence was selected to overlap with the survey mailing, but precede the study intervention. Analysis of the preceding 6-month period (i.e., May 20, 2006 through November 20, 2006) showed that adherence was not significantly different for these individuals when compared with the observation period ($P = 0.66$), supporting the stability of these measures over time.

Survey Administration and Design

The survey was mailed to all study participants beginning May 21, 2007. This self-administered survey contained questions pertaining to each participant's sociodemographics, perceptions and beliefs, knowledge regarding asthma and the medications used to treat asthma, interactions with the health care system, and social and environmental stressors and support.

To simplify, we organized these variables into internal (i.e., those pertaining to patient beliefs, knowledge, motivation regarding asthma and asthma treatments) and external factors (i.e., those pertaining to socioeconomic status; potential barriers to care, such as prescription co-pay and access to appointments; patient-physician communication; social support; and other external stressors, such as discrimination and crime exposure). The survey also collected information regarding the patients' age, self-identified race and ethnicity, duration of asthma, and underlining asthma control. Asthma control was assessed via the Asthma Control Test (QualityMetric Inc., Lincoln, RI) (17). For survey respondents, racial categories were assigned according to the patient's self-identified race. Demographic information for survey nonrespondents was obtained through data maintained by the health system. Whenever possible, we used a complete previously validated metric in the survey to assess each domain of interest. If a validated metric was not available we used metrics commonly used and reported in the literature.

For internal factors, we further subdivided our variables into the following categories: measures related to perception (18) and knowledge (19) about disease; beliefs (i.e., necessity and concern) about (20), knowledge of (21), and past experience with controller medication; the perceived locus of control over asthma, such as internal, chance, powerful others, and god (22, 23); self-efficacy (14); readiness to change (14); depression (24); and the personal importance of physician trust. *Past experience with controller medications* and the *personal importance of physician approval* were not previously validated

metrics. Past experience with controller medications asked the patient to rate the statements, "I have had good results using inhaled steroids in the past" and "In the past, my steroid inhaler has helped me control my asthma," on a 5-point Likert scale with the categories of strongly agree, agree, uncertain, disagree, and strongly disagree. The responses to these two statements were summed, with higher scores representing stronger agreement (range, 2–10). Personal importance of physician trust asked the patient to rate the statements, "It is important to me that my physician trusts me" and "It is important to me that my doctor knows that I am taking my asthma medications as prescribed" on the same 5-point Likert scale. The responses to these two statements were also summed, with higher scores representing stronger agreement (range, 2–10).

For external factors, we further subdivided our variables into the following categories: household income; wealth (i.e., home ownership and home value); highest level of education for the head of household; barriers to receiving care (e.g., difficulty getting to the doctor's office, difficulty in scheduling an appointment, or unable to afford the clinic visit) (25); medication co-payment and affordability; patient-clinician communication (21); social support and stressors (26); perceived discrimination (27); and exposure to crime and violence (28).

Statistical Analysis

We used general estimating equations to estimate the relationship between both internal and external factors and the continuous dependent variable, ICS adherence. We restricted our analysis to patients reporting African-American or white race-ethnicity, as these groups composed most of our patient population. Persons reporting other or multiple races were categorized as "other" and not included in the regression analyses. All regression models contained base variables for age in years, sex, self-reported race-ethnicity (i.e., African-American versus white), duration of asthma in years, and asthma control. In particular, we were interested to assess whether internal factors, external factors, or both mitigated the relationship between race-ethnicity and ICS adherence. We were also interested in the proportion of the variance in CMA explained by base variables, internal variables, and external variables. To compare the models, we also calculated the root mean squared error (RMSE), a measure of the difference between the estimator variables and the variable being estimated (i.e., adherence). Therefore, the model with the smallest RMSE is considered to have the best fit for the number of variables used.

We used forward stepwise regression to identify those characteristics associated with ICS medication adherence for the entire study population and stratified by race-ethnicity. We required these models to include the base variables of age, sex, race-ethnicity (except where stratified by race), duration of asthma, and asthma control. These models then identified those variables representing internal and external factors that were associated with adherence. At each step the variable with the smallest P value was included in the model, provided the P value was < 0.05. The procedure stops when there are no further variables with a P value < 0.05.

As *post hoc* analyses, we also included use of other asthma controller medications (i.e., long-acting β -agonists, methylxanthines, mast cell stabilizers, leukotriene inhibitors, and omalizumab) as a covariate in our regression models. Using the entire analytic cohort, we also assessed for interactions with race-ethnicity for those variables significantly associated with ICS adherence and potentially differing between African-American and white patients. All analyses were performed using SAS v9.1 (SAS Institute Inc., Cary, NC.)

RESULTS

Surveys were sent to 1,833 adult patients based on their apparent study eligibility; however, 46 (2.5%) were found to be ineligible because they denied a prior physician diagnosis of asthma. Of the remaining 1,787 patients, 1,006 (56.3%) returned their survey. The characteristics of the 1,006 survey respondents and the 753 nonrespondents are shown in Table 1. Nonrespondents tended to be younger, male, and of nonwhite race-ethnicity when compared with survey respondents. The former

TABLE 1. CHARACTERISTICS OF SURVEY RESPONDENTS AND NON-RESPONDENTS

	Survey Respondents (n = 1,006)	Survey Nonrespondents (n = 753)	P Value*
Age, yr, mean $\pm$ SD [†]	43.1 $\pm$ 10.4	37.7 $\pm$ 11.9	0.001
Female, no. (%)	716 (71.2)	458 (60.8)	0.001
Race-ethnicity, no. (%) [‡]			0.001
African-American	336 (33.4)	320 (42.5)	—
White	614 (61.0)	380 (50.5)	—
Other	56 (5.6)	53 (7.0)	—
Duration of asthma, yr, mean $\pm$ SD [§]	18.3 $\pm$ 14.0	—	—
Asthma Control Test score, mean $\pm$ SD	19.9 $\pm$ 4.2	—	—
Controller therapy used during observation period, no. (%)			0.001
Inhaled corticosteroid alone	417 (41.4)	407 (54.1%)	
Inhaled corticosteroid with additional controller medication [¶]	589 (58.6)	346 (45.9%)	
Percent inhaled corticosteroid adherence, mean $\pm$ SD**	36.6 $\pm$ 34.4	25.0 $\pm$ 28.6	0.001

* P value is for the comparison of survey respondents vs. nonrespondents.

[†] The number of individuals with data is 1,006 and 753, respectively.

[‡] The race-ethnicity categories for survey respondents were taken from the survey, and hence are self-reported. The categories for survey nonrespondents were obtained from the electronic medical record.

[§] The number of individuals with data is 916.

^{||} From the Asthma Control Test, where higher scores reflect better asthma control (range, 5–25) (17). The number of individuals with data is 932.

[¶] Other asthma controller medications include long-acting β -agonists, methylxanthines, mast cell stabilizers, leukotriene inhibitors, and omalizumab.

** The number of individuals with data is 977 and 739, respectively.

were also less likely to use additional asthma controller therapies, and they had lower ICS adherence.

The conceptual model for the base, internal, and external predictors of ICS adherence are shown in Figure 1. Table 2 shows the relationship between the base variables and ICS adherence before and after adjusting for internal and external factors. Individuals who reported being of African-American race-ethnicity had lower ICS adherence when compared with

self-reported white patients. However, adjustment for internal factors, but not external factors, markedly diminished the relationship between adherence and race-ethnicity, suggesting that one or more of the internal factors may account for the difference in adherence by race-ethnicity. Increasing age was associated with better ICS adherence, and this relationship was also diminished after accounting for internal factors. In contrast, adherence was also found to be lower among both women (as compared with men) and those with better asthma control, and these relationships were largely unaffected by adjusting for internal and external factors. Examination of model fit parameters suggested that the biggest gain in the explained variance of ICS adherence (i.e., largest increase in R^2) came from the internal factors, and that inclusion of these variables also created more parsimonious models (i.e., lower error of approximation per degree of freedom), as evidenced by the lower RMSE.

As we were interested in factors associated with ICS adherence, and in particular among African-American patients and white patients separately, we used forward stepwise regression to identify those factors associated with adherence before and after stratifying by race-ethnicity. These models also adjusted for all of the base variables. The resulting models shown in Tables 3, 4, and 5 were used to identify internal factors, external factors, or both, respectively.

Table 3 shows the forward stepwise regression models to identify internal factors associated with ICS adherence. When all patients were analyzed together, perceived necessity of inhaled steroids, knowledge about inhaled steroids, and readiness to take inhaled steroids were all significantly and positively associated with ICS adherence. Together these variables accounted for 14.1% of the variation in ICS adherence beyond that explained by the base variables (i.e., partial R^2 0.141). However, the pattern of internal factors associated with ICS adherence was quite different among white and African-American patients. For example, among white patients, most of the aforementioned factors were also significant, including the perceived necessity of inhaled steroids, knowledge about inhaled steroids, and readiness to take inhaled steroids. A perception by patients that doctors were the source of asthma control was also associated with higher adherence among white patients. Together these internal variables accounted for 19.8% of the variation in

Figure 1. Conceptual model of the base, internal, and external factors potentially related to adherence to inhaled corticosteroids among patients with asthma.

TABLE 2. RELATIONSHIP BETWEEN BASE, INTERNAL, AND EXTERNAL FACTORS AND INHALED CORTICOSTEROID ADHERENCE

	Base Variables Only*		Base Variables and Internal Factors [†]		Base Variables and External Factors [‡]		Base Variables and both Internal and External Factors [§]	
	% Change in Adherence ± SE	P Value	% Change in Adherence ± SE	P Value	% Change in Adherence ± SE	P Value	% Change in Adherence ± SE	P Value
Age, yr	6.7 ± 1.7	0.001	3.9 ± 1.7	0.019	6.2 ± 1.8	0.001	4.0 ± 1.7	0.022
Female sex [¶]	−8.5 ± 3.5	0.016	−9.5 ± 3.4	0.006	−9.6 ± 3.7	0.010	−10.8 ± 3.6	0.003
African- American race-ethnicity ^{**}	−11.5 ± 3.6	0.002	−3.4 ± 3.7	0.362	−13.9 ± 4.7	0.003	−4.7 ± 4.7	0.322
Duration of asthma ^{††}	0.01 ± 0.1	0.935	−0.1 ± 0.1	0.258	0.02 ± 0.1	0.842	−0.1 ± 0.1	0.262
Asthma control ^{‡‡}	−0.8 ± 0.4	0.040	−0.9 ± 0.5	0.055	−1.0 ± 0.4	0.015	−0.9 ± 0.5	0.046
Model R ² ^{§§}	0.072		0.225		0.124		0.266	
Model RMSE	0.345		0.321		0.343		0.320	

Definition of abbreviation: RMSE = root mean square error.

* Adjusted for all variables shown (i.e., the base variables as also shown in Figure 1).

† Adjusted for all the variables shown plus the internal factors, which include perception (18) and knowledge (19) about asthma; beliefs about the necessity of (20), concerns about (20), knowledge of (21), and past experience with asthma controller medication; perceived locus of control over asthma (i.e., internal, chance, powerful others, and god) (22, 23); confidence in ability to take controller medication (i.e., self-efficacy) (14); readiness to take controller medication as prescribed (14); personal importance of physician trust; and depression (24).

‡ Adjusted for all the variables shown plus the external factors, which include variables for socioeconomic status (i.e., household income, wealth [home ownership and home value], and highest level of education for the head of household); barriers to receiving care (i.e., variables for clinic not open at times needed, difficulty in getting to physician's office, couldn't get a timely appointment, long clinic wait to see physician, and couldn't afford clinical visit) (25); barriers to obtaining medication (i.e., variables representing co-payment amount and patient-reported difficulty affording medication); patient-clinician communication (21); level of social support and stressors (e.g., from family, friends, neighbors, etc.) (26); perceived discrimination (27); and exposure to crime and/or violence (28).

§ Adjusted for all the variables shown plus all the internal and external factors listed.

|| Per 10-yr increments in age.

¶ As compared with males.

** As compared with individuals whose self-reported race was white.

†† Per 1-yr increase in asthma duration.

‡‡ Per 1-unit increase in patient responses to the Asthma Control Test (test range, 5–25), with increasing values indicative of better control (17).

§§ Model R² refers to the proportion of the variance in adherence explained by the variables included in the model. Higher values indicate that the variables explain a larger proportion of the variance.

||| Model root mean square error is a measure of the difference between the estimator variables and the variable being estimated (i.e., adherence). The model with the smallest RMSE is considered to have the best fit for the number of variables used.

ICS adherence among white patients after accounting for the base variables. In contrast, readiness to take inhaled steroids was the only internal factor found to be significantly associated with ICS adherence among African-American patients. This variable accounted for 5.6% of the variation in ICS adherence among African-American patients after accounting for base variables.

The relationship between external factors and ICS adherence was also different among African-American and white patients (Table 4). Among African-American patients, only household income was associated with ICS adherence (each \$10,000 increase in household income was associated with a 1.8% increase in adherence). This variable accounted for 3.2% of the variation in ICS adherence among African-American patients after accounting for base variables. Among white patients, reported difficulty in affording medication and long clinic waits to see physicians were negatively associated with ICS adherence, whereas higher patient-clinician communication scores were positively associated with ICS adherence. Together these external factors accounted for 5.8% of the variation in ICS adherence among white patients after accounting for the base variables.

Table 5 shows the results of the forward stepwise regression models selecting both internal and external variables. The observed pattern among African-American and white patients was again quite different, but reflective of the earlier stepwise models. Among white patients, perceived necessity of inhaled steroids, knowledge about inhaled steroids, doctors being perceived as the source of asthma control, readiness to take inhaled steroids, reported difficulty in affording medication, long clinic waits to see physicians and were also significantly associated with ICS adherence. Together these variables accounted for 23.1% of the variation in ICS adherence among white patients after accounting for the base variables. In

contrast, only readiness to take inhaled steroids was found to be significantly associated with ICS adherence among African-American patients in the stepwise models including both internal and external factors. Again, this variable accounted for 5.6% of the variation in ICS adherence among African-American patients after accounting for the base variables.

There also appeared to be other consistent associations in the regression models stratified by race-ethnicity (Tables 3, 4, and 5). Notably, among African-American patients, increasing age was positively associated with ICS adherence, such that a 10-year increase in age was associated with an approximate 7% absolute increase in ICS adherence. Also, white women appeared to have significantly lower ICS adherence when compared with white men (i.e., an approximate 8% absolute difference in ICS adherence).

As a *post hoc* analysis we also adjusted for the use of other controller medications. This adjustment had no substantive impact on the factors associated with ICS adherence. We also assessed for interactions with race-ethnicity for those variables significantly associated with ICS adherence and potentially differing between African-American and white patients (data not shown). The interaction terms were statistically significant or borderline significant for perceived necessity of inhaled steroids ($P = 0.023$), knowledge about inhaled steroids ($P = 0.061$), doctors being perceived as the source of asthma control ($P = 0.110$), further supporting a difference by race-ethnicity.

DISCUSSION

Many external and internal factors have been shown to be associated with patient ICS adherence, yet their relative importance

TABLE 3. FORWARD STEPWISE REGRESSION OF INTERNAL FACTORS ASSOCIATED WITH ADHERENCE STRATIFIED BY SELF-REPORTED RACE-ETHNICITY

	All Patients		African-American Patients		White Patients	
	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value
Base variables*						
Age [†]	4.4 $\pm$ 1.6	0.008	7.7 $\pm$ 2.9	0.009	2.5 $\pm$ 2.0	0.203
Female sex [‡]	-8.5 $\pm$ 3.3	0.011	-10.3 $\pm$ 5.9	0.082	-8.4 $\pm$ 3.9	0.034
African- American race-ethnicity [§]	-3.6 $\pm$ 3.5	0.302	—	—	—	—
Duration of asthma	-0.1 $\pm$ 0.1	0.316	-0.0 $\pm$ 0.2	0.799	-0.1 $\pm$ 0.1	0.559
Asthma control [¶]	-0.5 $\pm$ 0.4	0.179	-0.2 $\pm$ 0.6	0.781	-0.9 $\pm$ 0.5	0.058
Internal variables selected						
Perceived necessity of asthma medication**	1.7 $\pm$ 0.4	0.001			2.0 $\pm$ 0.5	0.001
Knowledge of asthma medication ^{††}	1.4 $\pm$ 0.3	0.001			1.7 $\pm$ 0.4	0.001
Doctor as the perceived locus of control for asthma ^{‡‡}					1.7 $\pm$ 0.8	0.030
Readiness to take controller medication as prescribed ^{§§}	2.4 $\pm$ 0.6	0.001	2.5 $\pm$ 0.9	0.007	2.3 $\pm$ 0.8	0.007
Model R ²	0.203		0.136		0.235	
Partial R ² ^{¶¶}	0.141		0.056		0.198	

* Base variables (i.e., age, sex, duration of asthma, and asthma control) with the exception of race-ethnicity were kept in the stepwise regression models. Therefore, the internal variables selected are those remaining significant after adjusting for base variables. A variable for race-ethnicity was included in the model with all patients, but not in the two models stratified by race-ethnicity.

[†] Per 10-yr increments in age.

[‡] As compared with males.

[§] As compared with individuals whose self-reported race was white.

^{||} Per 1-yr increase in asthma duration.

[¶] Per 1-unit increase in patient responses to the Asthma Control Test (test range, 5–25), with increasing values indicative of better control (17).

** Necessity score from the Belief in Medication Questionnaire where increasing values associated with increasing perceived necessity of medication (scores range from 5–25) (20).

^{††} Knowledge of medication adapted from the study by Apter and colleagues, in which increasing values were associated with increasing knowledge of the function and effects of inhaled corticosteroids (scores range from 6–30) (21).

^{‡‡} Adapted from the Multidimensional Health Locus of Control Scales (23). Higher scores on the doctor domain of this metric imply that a patient perceives their doctor to have a greater influence on their asthma control (scores for the doctor domain range from 3–18).

^{§§} Readiness to take controller medication as prescribed metric adapted from the study by Schmalzing and coworkers, in which increasing values were associated with increasing readiness to take inhaled steroids as prescribed (scores range from 1–10) (14).

^{|||} Model R² refers to the proportion of the variance in adherence explained by all the variables included in the model. Higher values indicate that the variables explain a larger proportion of the variance.

^{¶¶} Partial R² refers to the proportion of variance in adherence explained by the internal variables selected in the forward stepwise regression beyond that explained by the base variables.

was largely unknown. In this study, we found that internal factors (i.e., those pertaining to patient beliefs, knowledge, motivation regarding asthma, and asthma treatments) explained a larger proportion of the variance in adherence when compared with external factors (i.e., those pertaining to socioeconomic status; potential barriers to care, such as prescription co-pay and access to appointments; patient–physician communication; social support; and other external stressors, such as discrimination and crime exposure). Moreover, we found that the set of factors associated with medication adherence was different among African-American and white patients.

Studying a diverse group of 85 adult patients with asthma, Apter and coworkers (5) examined the relationship between ICS adherence and both immutable factors (i.e., age, sex, race-ethnicity, education, insurance status, household income, smoking, asthma severity, and past adherence) and mutable factors (i.e., knowledge, patient–physician communication, social support, depression, and attitude). African-American race-ethnicity and patient attitude (defined as stronger beliefs in the benefits and safety of inhaled steroids) were consistently negatively and positively associated with ICS adherence, respectively. However, patient attitude alone was insufficient to account for differences by race-ethnicity. Recently, Le and

colleagues reported the findings from a study of 86 adults with asthma, where a similar construct for ICS beliefs mitigated the relationship between minority status and adherence (29). In the current study, we found that adjusting for internal factors, including medication beliefs, diminished the relationship between race-ethnicity and adherence.

Multiple behavioral models have been proffered to describe components contributing to patient medication adherence (11–13, 30–32). Accordingly, we adapted elements from Social Learning Theory, the Health Beliefs Model, and the Trans-theoretical Model to develop, *a priori*, a model that we believed contained conceptually distinct elements potentially predictive of adherence (Figure 1). Curiously, only readiness to take inhaled steroids, a measure reflective of the Transtheoretical Model (14), was associated with adherence in both African-American and white patients with asthma. In fact, readiness to take ICS medication was the only factor consistently associated with medication adherence in African-American patients. These findings are supported by those of Schmalzing and coworkers, who noted that individuals in more committed stages of change (i.e., action and maintenance stages) had higher adherence when compared with individuals in pre-contemplation, contemplation, or preparation stages (14).

TABLE 4. FORWARD STEPWISE REGRESSION OF EXTERNAL FACTORS ASSOCIATED WITH ADHERENCE STRATIFIED BY SELF-REPORTED RACE-ETHNICITY

	All Patients		African-American Patients		White Patients	
	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value
Base variables*						
Age [†]	5.7 $\pm$ 1.7	0.001	7.6 $\pm$ 2.9	0.011	4.6 $\pm$ 2.1	0.026
Female sex [‡]	−9.3 $\pm$ 3.5	0.009	−9.9 $\pm$ 6.0	0.103	−8.9 $\pm$ 4.3	0.039
African-American race-ethnicity [§]	−10.8 $\pm$ 3.6	0.003	—	—	—	—
Duration of asthma	0.0 $\pm$ 0.1	0.743	−0.1 $\pm$ 0.2	0.726	0.1 $\pm$ 0.2	0.614
Asthma control [¶]	−1.0 $\pm$ 0.4	0.012	−0.6 $\pm$ 0.6	0.335	−1.4 $\pm$ 0.5	0.006
External variables selected						
Reported difficulty affording medication**	−13.4 $\pm$ 6.4	0.036			−25.6 $\pm$ 10.3	0.013
Long clinic wait to see physician ^{††}	−12.0 $\pm$ 6.1	0.050			−17.3 $\pm$ 7.2	0.017
Patient-clinician communication ^{‡‡}	1.0 $\pm$ 0.5	0.027			1.5 $\pm$ 0.6	0.009
Household income ^{§§}			1.8 $\pm$ 0.9	0.043		
Model R ²	0.103		0.114		0.102	
Partial R ² ^{¶¶}	0.033		0.032		0.058	

* Base variables (i.e., age, sex, duration of asthma, and asthma control) with the exception of race-ethnicity were kept in the stepwise regression models. Therefore, the external variables selected are those remaining significant after adjusting for base variables. A variable for race-ethnicity was included in the model with all patients, but not in the two models stratified by race-ethnicity.

[†] Per 10-yr increments in age.

[‡] As compared with males.

[§] As compared with individuals whose self-reported race was white.

^{||} Per 1-yr increase in asthma duration.

[¶] Per 1-unit increase in patient responses to the Asthma Control Test (test range, 5–25), with increasing values indicative of better control (17).

** Patient-reported difficulty affording medication (yes = 1, no = 0).

^{††} Patient-reported long clinic wait to see physician (yes = 1, no = 0) (25).

^{‡‡} Patient-clinician communication adapted from the study by Apter and colleagues, in which increasing values were associated with better communication (scores range from 6–30) (21).

^{§§} Per \$10,000 increase in household income.

^{|||} Model R² refers to the proportion of the variance in adherence explained by all the variables included in the model. Higher values indicate that the variables explain a larger proportion of the variance.

^{¶¶} Partial R² refers to the proportion of variance in adherence explained by the external variables selected in the forward stepwise regression beyond that explained by the base variables.

The finding that “readiness” was a common factor among both African-American and white patients suggests that appropriately targeted interventions may improve adherence in both groups. Motivational interviewing (MI) may be such an intervention. Using this technique, a healthcare provider asks nonthreatening open-ended questions in an attempt to foster intrinsic motivation in patients ambivalent to change (33). MI has been shown to improve adherence to antiretroviral medications in a cohort of low-income men and women with HIV (34) and to a diet and exercise regimen among overweight women with type 2 diabetes (35).

In addition to readiness to take inhaled steroids, we also found that perceived necessity of inhaled steroids; knowledge about inhaled steroids; and a perception that doctors were an important source of asthma control were all positively associated with ICS adherence among white patients. These findings underscore the importance of assessing the behavioral model on which interventions are based in the target population, since these relationships may differ between groups.

This study must be interpreted in light of its limitations. First, despite the many base, internal, and external factors assessed, together these variables explained at most 26% of the variance in ICS adherence. This suggests that other important factors exist and were not assessed. Perhaps this also reflects a high proportion of unintentional nonadherence, whereby patients do not realize that they are being nonadherent and which would not be necessarily associated with the factors assessed.

Second, all of the patients in our study population had health insurance, and therefore tacit access to health care and medi-

cation. Yet even in this covered population, reporting difficulty affording medication was associated with lower ICS use among white patients, similar to that reported elsewhere (36). However, consistent with our earlier findings, adherence did not appear to be strongly related to the amount of medication copayment (2). As uninsured adults have been shown to be nearly twice as likely to report failing to fill a prescription due to cost when compared with insured adults with prescription coverage (37), it might be expected that external factors, such as cost of medications or household income, might influence adherence to a greater extent in patients without such coverage. Therefore, while our findings may not apply to the uninsured, they still may apply to the majority of nonelderly U.S. adults who happen to possess prescription coverage (37).

We also demonstrated that survey nonresponders differed from those individuals who completed the survey, in that the former were more likely to be African American, male, and younger in age. Differences in ICS adherence between respondents and nonrespondents were still present after stratifying by race-ethnicity (data not shown). Therefore, despite the large number of individuals studied, the factors associated with adherence in survey nonrespondents may have differed from those who returned their survey. This may explain why, in an earlier study not dependent on patient survey responses, we also found neighborhood factors such as crime rates to be associated with ICS adherence (2).

Lastly, our metrics of adherence reflected average use over a 6-month period. While we have previously shown that these metrics are predictive of asthma outcomes (1, 3), they cannot

TABLE 5. FORWARD STEPWISE REGRESSION OF INTERNAL AND EXTERNAL FACTORS ASSOCIATED WITH ADHERENCE STRATIFIED BY SELF-REPORTED RACE-ETHNICITY

	All Patients		African-American Patients		White Patients	
	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value	% Change in Adherence $\pm$ SE	P Value
Base variables*						
Age [†]	3.7 $\pm$ 1.6	0.022	7.7 $\pm$ 2.9	0.009	1.9 $\pm$ 1.9	0.338
Female sex [‡]	-8.1 $\pm$ 3.3	0.014	-10.3 $\pm$ 5.9	0.082	-8.5 $\pm$ 3.9	0.029
African-American race-ethnicity [§]	-2.6 $\pm$ 3.5	0.471	—	—	—	—
Duration of asthma	-0.1 $\pm$ 0.1	0.370	-0.0 $\pm$ 0.2	0.799	-0.0 $\pm$ 0.1	0.815
Asthma control [¶]	-0.7 $\pm$ 0.4	0.082	-0.2 $\pm$ 0.6	0.781	-1.3 $\pm$ 0.5	0.013
Internal and external variables selected						
Perceived necessity of asthma medication**	1.8 $\pm$ 0.4	0.001			2.0 $\pm$ 0.4	0.001
Knowledge of asthma medication ^{††}	1.3 $\pm$ 0.3	0.001			1.7 $\pm$ 0.4	0.001
Doctor as the perceived locus of control for asthma ^{‡‡}					2.0 $\pm$ 0.8	0.011
Readiness to take controller medication as prescribed ^{§§}	2.1 $\pm$ 0.6	0.001	2.5 $\pm$ 0.9	0.007	2.0 $\pm$ 0.8	0.016
Reported difficulty affording medication	-13.5 $\pm$ 6.0	0.024			-23.7 $\pm$ 9.4	0.013
Inability to get an appointment when needed ^{¶¶}	-8.2 $\pm$ 3.9	0.037				
Long clinic wait to see physician ^{***}					-16.4 $\pm$ 6.6	0.013
Model R ^{2†††}	0.219		0.136		0.262	
Partial R ^{2‡‡‡}	0.158		0.056		0.231	

* Base variables (i.e., age, sex, duration of asthma, and asthma control) with the exception of race-ethnicity were kept in the stepwise regression models. Therefore, the internal and external variables selected are those remaining significant after adjusting for base variables. A variable for race-ethnicity was included in the model with all patients, but not in the two models stratified by race-ethnicity.

[†] Per 10-yr increments in age.

[‡] As compared with males.

[§] As compared with individuals whose self-reported race was white.

^{||} Per 1-yr increase in asthma duration.

[¶] Per 1-unit increase in patient responses to the Asthma Control Test (test range, 5–25), with increasing values indicative of better control (17).

** Necessity score from the Belief in Medication Questionnaire where increasing values associated with increasing perceived necessity of medication (scores range from 5–25) (20).

^{††} Knowledge of medication adapted from the study by Apter and coworkers, in which increasing values were associated with increasing knowledge of the function and effects of inhaled corticosteroids (scores range from 6–30) (21).

^{‡‡} Adapted from the Multidimensional Health Locus of Control Scales (23). Higher scores on the doctor domain of this metric imply that a patient perceives their doctor to have a greater influence on their asthma control (scores for the doctor domain range from 3–18).

^{§§} Readiness to take controller medication as prescribed metric adapted from the study by Schmalzing and colleagues, in which increasing values were associated with increasing readiness to take inhaled steroids as prescribed (scores range from 1–10) (14).

^{|||} Patient-reported difficulty affording medication (yes = 1, no = 0).

^{¶¶} Patient-reported being unable to get an appointment with physician when needed (yes = 1, no = 0) (25).

^{***} Patient-reported long clinic wait to see physician (yes = 1, no = 0) (25).

^{†††} Model R² refers to the proportion of the variance in adherence explained by all the variables included in the model. Higher values indicate that the variables explain a larger proportion of the variance.

^{‡‡‡} Partial R² refers to the proportion of variance in adherence explained by the internal and external variables selected in the forward stepwise regression beyond that explained by the base variables.

assess patterns of daily ICS use which may have different associations with internal and external factors. Adherence measures based on pharmacy claims also do not assess appropriateness of treatment, although we did adjust for self-reported asthma control in all of our regression models.

In summary, we found that internal factors (i.e., those pertaining to patient beliefs, knowledge, motivation regarding asthma, and asthma treatments), explained the largest proportion of the variance in adherence, and that accounting for these factors diminished the observed association between race-ethnicity and adherence. Given the disappointing results of most interventions to improve adherence to date, understanding the factors associated with nonadherence and how they differ by race-ethnicity may help us design more effective interventions in the future (38, 39). While this study represents another step in that direction, the modest amount of overall variance explained suggests that more work is still needed to identify additional contributing factors.

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