

# Racial Disparities in HIV Virologic Failure: Do Missed Visits Matter?

Michael J. Mugavero, MD, MHSc,\* Hui-Yi Lin, PhD,† Jeroan J. Allison, MD, MSc,‡  
 Thomas P. Giordano, MD, MPH,§ James H. Willig, MD,\* James L. Raper, DSN, CRNP, JD,\*  
 Nelda P. Wray, MD, MPH,‡ Stephen R. Cole, PhD,|| Joseph E. Schumacher, PhD,‡  
 Susan Davies, PhD,¶ and Michael S. Saag, MD\*

**Background:** Racial/ethnic health care disparities are well described in people living with HIV/AIDS, although the processes underlying observed disparities are not well elucidated.

**Methods:** A retrospective analysis nested in the University of Alabama at Birmingham 1917 Clinic Cohort observational HIV study evaluated patients between August 2004 and January 2007. Factors associated with appointment nonadherence, a proportion of missed outpatient visits, were evaluated. Next, the role of appointment nonadherence in explaining the relationship between African American race and virologic failure (plasma HIV RNA >50 copies/mL) was examined using a staged multivariable modeling approach.

**Results:** Among 1221 participants, a broad distribution of appointment nonadherence was observed, with 40% of patients missing at least 1 in every 4 scheduled visits. The adjusted odds of appointment nonadherence were 1.85 times higher in African American patients compared with whites [95% confidence interval (CI) = 1.61 to 2.14]. Appointment nonadherence was associated with virologic failure (odds ratio = 1.78, 95% CI = 1.48 to 2.13) and partially mediated the relationship between African American race and virologic failure. African Americans had 1.56 times the adjusted odds of virologic

failure (95% CI = 1.19 to 2.05), which declined to 1.30 (95% CI = 0.98 to 1.72) when controlling for appointment nonadherence, a hypothesized mediator.

**Conclusions:** Appointment nonadherence was more common in African American patients, associated with virologic failure, and seemed to explain part of observed racial disparities in virologic failure.

**Key Words:** access to care, adherence, disparities, HIV/AIDS, mediation

(*J Acquir Immune Defic Syndr* 2009;50:100–108)

## INTRODUCTION

Racial/ethnic disparities in health care [eg, antiretroviral (ARV) medication receipt] and clinical outcomes (eg, mortality) are well described in people living with HIV/AIDS,<sup>1–3</sup> although the processes underlying observed disparities have not been well elucidated. Recently, there has been a call for the research community to move beyond descriptive studies in an effort to gain a better understanding of the root causes contributing to health care disparities.<sup>4–6</sup> It has been argued that investigation of pathways mediating disparities has been limited thus impeding intervention development. Although such pathways are likely to be complex and multifaceted, a better understanding of contributing factors is needed to inform evidence-based interventions that will effectively address health care disparities.<sup>4,5,7</sup>

One particularly important pathway is access to care, which has long been recognized as an important factor contributing to health care disparities.<sup>7–11</sup> Although insurance coverage is a known contributor, the Institute of Medicine reported that disparities in the quantity and quality of care exist even for patients with similar insurance coverage.<sup>8</sup> To date, the role of detailed measures of access to care as a component of the pathway contributing to disparities in health care processes and outcomes has not been extensively studied, particularly when adjusting for insurance status. One such detailed measure is adherence to scheduled outpatient appointments among patients engaged in medical care.

Appointment nonadherence, or missed outpatient appointments, are common in HIV-infected patients and have been observed more frequently in African Americans and the

Received for publication May 2, 2008; accepted September 10, 2008.

From the \*Division of Infectious Diseases; †Medical Statistics Section; ‡Division of Preventive Medicine, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL; §Sections of Infectious Diseases and Health Services Research, Department of Medicine, Baylor College of Medicine, Houston, TX; ||Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; and ¶Department of Health Behavior, University of Alabama at Birmingham, Birmingham, AL.

Supported by the University of Alabama at Birmingham 1917 Clinic Cohort which receives financial support from the following: University of Alabama at Birmingham Center for AIDS Research (CFAR, grant P30-AI27767), CFAR-Network of Integrated Clinical Systems (grant 1 R24 AI067039-1), and the Mary Fisher Clinical AIDS Research and Education (CARE) Fund. This study was supported by grant number K23MH082641 from the National Institute of Mental Health (M.J.M.).

Presented in part at the 45th Annual Meeting of the Infectious Diseases Society of America, October 4–7, 2007, San Diego, CA and at the Society of Behavioral Medicine's 29th Annual Meeting and Scientific Sessions, March 26–29, 2008, San Diego, CA.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health or the National Institutes of Health.

Correspondence to: Michael J. Mugavero, MD, MHSc, CCB 142, 908 20th Street South, Birmingham, AL 35294-2050 (e-mail: mmugavero@uab.edu).  
 Copyright © 2008 by Lippincott Williams & Wilkins

uninsured.<sup>12–15</sup> Missed visits have also been associated with a higher incidence of virologic failure and clinical disease progression including incident AIDS-defining illnesses and death.<sup>16–22</sup> However, to our knowledge, the potential role of appointment nonadherence in contributing to racial/ethnic disparities in HIV outcomes has not been well studied. Therefore, we conducted this study to evaluate the role of appointment nonadherence in explaining, in part, observed racial disparities in virologic failure in an outpatient HIV cohort engaged in clinical care.

## METHODS

### Sample and Procedure

The University of Alabama at Birmingham (UAB) 1917 Clinic Cohort is an Institutional Review Board (IRB) approved HIV clinical cohort protocol for the conduct of retrospective and prospective studies that has been described previously ([www.uab1917cliniccohort.org](http://www.uab1917cliniccohort.org)).<sup>23–25</sup> Established in 1992, the cohort contains detailed sociodemographic, psychosocial, and clinical information from all patients receiving care at the UAB 1917 HIV/AIDS Clinic, including over 1500 active patients. The current study includes patients with  $\geq 4$  scheduled primary HIV care appointments occurring over a minimum of 6 months between the first and last appointment ( $\geq 6$  months) at the UAB 1917 HIV/AIDS Clinic during the study period of August 1, 2004 to January 31, 2007. Consistent with previous research,<sup>12,13,26,27</sup> appointments “canceled” by the patient in advance of the scheduled visit or due to hospitalization, and visits canceled by the 1917 Clinic, were excluded from the scheduled appointment measure as were all subspecialty appointments at the clinic (eg, dermatology).

### Measures

#### Appointment Nonadherence

A missed visit proportion (MVP) was calculated for all study participants as a ratio of the number of “no show” visits divided by the overall number of scheduled appointments (“arrived” and “no show”) during the study period.

#### ARV Receipt During the Study Period

Consistent with prior studies,<sup>28–30</sup> and with treatment recommendations at the time of the study,<sup>31</sup> patients who received ARVs and those with a laboratory indication for ARV therapy (CD4 < 350 cells/mm<sup>3</sup> and/or plasma HIV RNA > 100,000 copies/mL) at any point during the study period were included in these analyses.

#### Virologic Failure—Failure to Achieve an Undetectable Plasma HIV RNA (<50 Copies/mL)

Among patients receiving ARVs during the study period, the last plasma HIV RNA level [viral load (VL)] obtained during the study period was evaluated and recorded as a dichotomous measure (<50 copies/mL vs.  $\geq 50$  copies/mL). The last VL measure was chosen to evaluate the temporal role of appointment nonadherence on subsequent virologic failure.

To be included in this analysis, the last VL measure had to be obtained at least 90 days after each patient’s first attended visit during the study period.

### Other Measures

Sociodemographic characteristics, comorbid affective mental health disorders, substance abuse and alcohol abuse disorders as recorded in patients’ medical record, and baseline CD4 count, defined as the most recent measure within  $\pm 90$  days of the initial clinic visit during the study period, were ascertained by query of the 1917 Clinic Database. Because only 29 (2%) patients belonged to a racial/ethnic group other than African American and white, these patients were excluded from analyses.

### Mediation Analysis

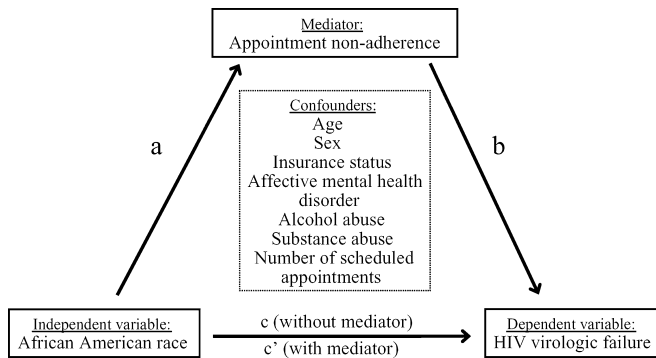
The application of mediation methods in the evaluation of observational data has a long-standing history in the social sciences and is being employed increasingly in biomedical research.<sup>32–35</sup> Mediation analyses allow for the evaluation of pathways through which independent variables exert an effect on dependent variables. These methods are particularly germane when studying areas not amenable to randomized studies, such as health care disparities, because they allow for the identification of relevant pathways that may be targeted when developing informed interventions. A basic approach to mediation analysis involves a 3 variable system in which the role of a third variable (mediator) in contributing to the relationship between an independent and dependent variable is evaluated.<sup>32–35</sup> The current study employs this approach and evaluates the role of appointment nonadherence (mediator) in contributing to the relationship between African American race (independent variable) and HIV virologic failure (dependent variable) (Fig. 1).

According to this framework, a series of steps are required to conclude that mediation has occurred: (1) variations in the level of the independent variable significantly account for variations in the mediator (path a), (2) variations in the level of the mediator significantly account for variations in the level of the dependent variable (path b), (3) variations in the level of the independent variable significantly account for variations in the level of the dependent variable (path c), and (4) the effect of the independent variable on the dependent variable (path c’) is attenuated when the mediator is included in the equation.<sup>32–35</sup> Implicit in this framework is a temporal ordering whereby the potential mediator temporally follows the independent variable and temporally precedes the dependent variable. We believe that the temporal relationship between variables is correctly defined in this study. For this study, the 4 steps are evaluated in unadjusted analyses and when controlling for confounders, as described in the following section.

### Statistical Analysis

#### Association of Appointment Nonadherence With Patient Characteristics

Binomial generalized estimating equation models with an autoregressive correlation structure, which accounts for the correlation of multiple observations nested within each patient, were applied to generate the odds of a “no show” visit



**FIGURE 1.** Basic mediation model employed in the evaluation of appointment nonadherence as a mediator of racial disparities in HIV virologic failure (plasma HIV RNA > 50 copies/mL). According to this framework, a series of steps are required to conclude that mediation has occurred: (1) variations in the level of the independent variable significantly account for variations in the level of the mediator (path a, Table 1), (2) variations in the level of the mediator significantly account for variations in the level of the dependent variable (path b, Table 3), (3) variations in the level of the independent variable significantly account for variations in the level of the dependent variable (path c, Table 3), and (4) the effect of the independent variable on the dependent variable (path c', Table 3, last column) should be attenuated when the mediator (appointment nonadherence) is included in the equation.<sup>32–35</sup> Implicit in this framework is a temporal ordering whereby the potential mediator temporally follows the independent variable and temporally precedes the dependent variable. We believe the temporal relationship between variables is correctly defined in this study. For this study, the 4 steps are shown in both unadjusted analyses and when controlling for confounders, as displayed in the tables and described in the article.

for various patient characteristics. These analyses addressed step 1 (path a) of the mediation analysis.

### Predictors of ARV Medication Receipt

Unadjusted and multivariable logistic regression was applied to evaluate factors associated with failure to receive ARVs. Primary analyses included patients meeting study inclusion criteria (ie, those with  $\geq 4$  visits over  $\geq 6$  months), whereas sensitivity analyses were conducted using the entire clinic population who had at least 1 visit during the study period. Only patients treated with ARVs or with a laboratory indication for treatment were included in these analyses.

### Predictors of Virologic Failure: Staged Mediation Modeling

Factors associated with virologic failure (>50 copies/mL) were initially examined with unadjusted logistic regression models (paths b and c, unadjusted analyses).

To evaluate appointment nonadherence as a covariate potentially mediating the effects of a disparity marker (ie, African American race) on virologic failure, we used logistic regression to model virologic failure conditional on measured covariates to obtain the “total effects” (path c) and further conditional on appointment nonadherence to obtain the “direct

effects” (path c') using a basic mediation modeling approach (Fig. 1).<sup>32–35</sup> The first logistic regression model included all covariates except for MVP (path c, adjusted analysis). Next, a second model including MVP was used to evaluate the role of appointment nonadherence as a mediator of virologic failure, as indicated by shifts in parameter estimates and statistical significance for the African American race variable relative to the first model (path b, adjusted analysis and path c', mediation analysis). Such mediation assessments must assume that the mediator and outcome are not themselves confounded<sup>36,37</sup> and that the risk factor of interest and mediator do not interact to cause the outcome.<sup>37,38</sup>

Finally, we calculated the mediation ratio as  $(c-c')/c$ , which represented the estimated proportion of the association between the main exposure (African American race) and the outcome (virologic failure) attributable to the mediator (appointment nonadherence).<sup>32,39,40</sup> Following recommendations from Shroout and Bolger,<sup>40</sup> we generated 95% bias-corrected and accelerated confidence bands for the mediation ratio based on 1000 replicate datasets from random resampling with replacement (bootstrapping).

For each outcome measure, we examined interactions between the sex, race, and insurance variables and controlled for the total number of scheduled appointments in multivariable models. We also examined interactions between MVP and all other independent variables in the analysis of virologic failure. Sensitivity analyses were performed for all 3 outcome measures by restricting the sample to patients with  $\geq 4$  scheduled primary HIV care appointments occurring over  $\geq 12$  months, rather than the  $\geq 6$ -month period utilized for primary analyses. These analyses yielded similar results to the primary study analyses (data not shown). Statistical analyses were performed using SAS version 9.0 and STATA 10.0 SE.

## RESULTS

Among 1503 UAB 1917 HIV/AIDS Clinic patients with scheduled appointments during the study period, 1221 patients (81%) met study criteria and are included in this analysis. The mean age of study participants was 42.0 years, 24% were female, 47% were African American, 34% had public health insurance, and 23% were uninsured (Table 1). Half of study patients had an affective mental health disorder reported in their problem list, 19% had substance abuse disorders, and 13% had alcohol abuse disorders recorded in their medical records. The mean number of scheduled appointments (“arrived” and “no show” visits only) was 9.5 per patient during the 30-month study period.

A broad distribution of appointment nonadherence was observed with 40% of patients missing at least 1 of every 4 scheduled appointments (Fig. 2A). A higher median MVP was observed in younger patients, females, African Americans, patients lacking private health insurance, and those with alcohol abuse and substance abuse histories (Fig. 2B). In multivariable generalized estimating equation analysis, appointment nonadherence was associated with younger age, African American race [odds ratio (OR) = 1.85, 95% confidence interval (CI) = 1.61 to 2.14], having public health insurance,

**TABLE 1.** Overall Characteristics and Factors Associated With Poor Adherence to Primary HIV Care Appointments Among 1221 Patients With at Least 4 Scheduled Appointments Over a ≥6-Month Period at the UAB 1917 HIV/AIDS Clinic, August 2004 to January 2007\*

Characteristics	Mean ± SD or n (%)	Crude OR (95% CI) for No Show†	Adjusted OR (95% CI) for No Show†
Age (yrs)	42.0 ± 9.2	0.82 (0.76 to 0.88)‡§	0.86 (0.80 to 0.93)‡§
Sex			
Male	927 (75.9)	1.0	1.0
Female	294 (24.1)	1.34 (1.15 to 1.55)§	1.10 (0.94 to 1.29)
Race			
White	649 (53.1)	1.0	1.0
African American	572 (46.9)	2.00 (1.75 to 2.29)§	1.85 (1.61 to 2.14)§
Insurance			
Private	519 (42.5)	1.0	1.0
Public	416 (34.1)	1.58 (1.36 to 1.85)§	1.35 (1.16 to 1.58)§
Uninsured	286 (23.4)	1.54 (1.29 to 1.83)§	1.18 (0.99 to 1.41)
Affective mental health disorder			
No	615 (50.4)	1.0	1.0
Yes	606 (49.6)	0.89 (0.78 to 1.02)	0.93 (0.81 to 1.06)
Alcohol abuse			
No	1068 (87.5)	1.0	1.0
Yes	153 (12.5)	1.26 (1.03 to 1.55)¶	1.22 (1.01 to 1.48)¶
Substance abuse			
No	987 (80.8)	1.0	1.0
Yes	234 (19.2)	1.47 (1.25 to 1.73)§	1.38 (1.17 to 1.63)§
Baseline CD4 count (cells/mm <sup>3</sup> )			
≤200	318 (26.0)	1.35 (1.15 to 1.57)§	1.12 (0.96 to 1.32)
200–350	245 (21.1)	1.29 (1.08 to 1.54)§	1.22 (1.03 to 1.44)¶
>350	658 (53.9)	1.0	1.0
No. total appointments scheduled*	9.5 ± 3.7	—	—
MVP¶			
0%	373 (30.6)	—	—
0 < MVP < 25%	355 (29.1)	—	—
25 ≤ MVP < 50%	332 (27.2)	—	—
50 ≤ MVP < 75%	143 (11.7)	—	—
75 ≤ MVP < 100%	18 (1.5)	—	—

\*“No show” appointment status was modeled as the measure of poor adherence to HIV primary care appointments. All “arrived” and “no show” visits from all study participants during the study period were included in these analyses. “Canceled” visits, appointments not attended for which a patient notified the clinic they would miss the visit or was hospitalized, were excluded.

†Binomial generalized estimating equation models with an autoregressive correlation structure, which accounts for the correlation of multiple observations nested within each patient. Adjusted model controls for other variables with numeric values displayed in the table.

‡Odds ratio for 10 years increments.

§*P* < 0.01.

¶*P* < 0.05.

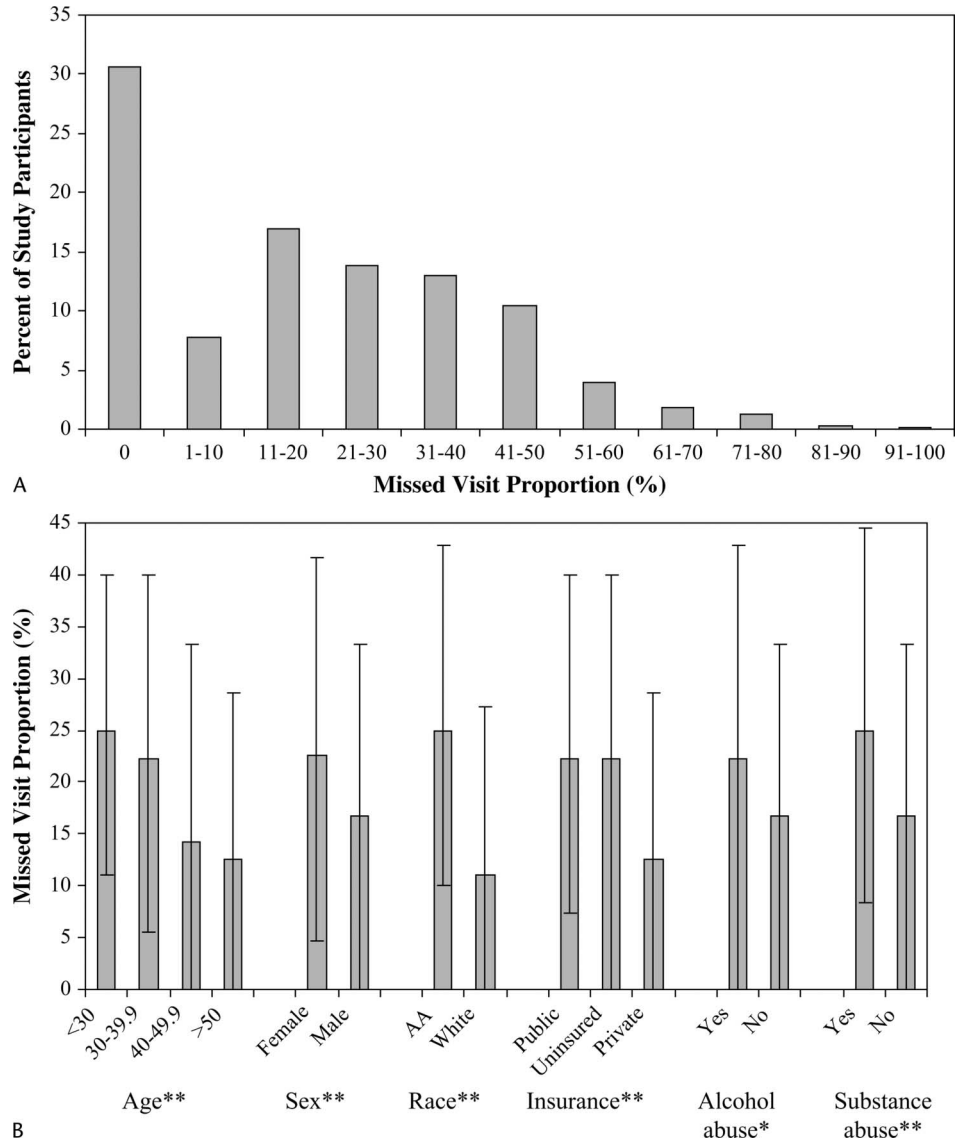
¶MVP is a binomial ratio of the number of “no show” visits divided by the overall number of scheduled appointments (“arrived” and “no show”) during the study period.

a baseline CD4 count of 200–350 cells per cubic millimeter, and alcohol abuse and substance abuse disorders (Table 1).

Among 1221 study participants, 1151 (94%) were eligible for ARV treatment during the study period, which was prescribed in 96% of these patients (1110/1151 individuals). In multivariable logistic regression analysis, only appointment nonadherence (OR = 2.03 per 25% MVP, 95% CI = 1.40 to 2.95) was associated with failure to have ARVs prescribed among treatment-eligible patients (Table 2). Sensitivity analysis evaluating all patients with an attended visit during the study period (N = 1503) found that 92% of treatment-eligible patients received ARVs. In multivariable analysis (excluding appointment nonadherence), African Americans (OR = 1.54,

95% CI = 1.00 to 2.39) and the uninsured (OR = 1.96, 95% CI = 1.16 to 3.3) were less likely to receive ARVs (data not shown).

Plasma HIV RNA levels obtained at least 90 days after the first attended visit in the study period were available for 1088 patients who received ARV therapy (98%). Forty-one percent of these patients (n = 448) experienced virologic failure (>50 copies/mL) at the last measure during the study period. In multivariable logistic regression analysis excluding appointment nonadherence (Table 3), younger age, African American race (OR = 1.56, 95% CI = 1.19 to 2.05), and having public health insurance were associated with virologic failure.



**FIGURE 2.** Distribution of appointment nonadherence as measured by the missed visit proportion (MVP), (2A) and characteristics associated with MVP in bivariate analyses (1B) among 1221 patients with at least 4 scheduled HIV primary care appointments over a  $\geq 6$ -month period at the UAB 1917 HIV/AIDS Clinic, August 2004 to January 2007. The median MVP and interquartile range is presented in Figure 2B and the nonparametric Kruskal–Wallis test was used to compare median MVP among study participants. \* $P < 0.05$ , \*\* $P < 0.01$  of Kruskal–Wallis test.

Subsequently, MVP was added to the multivariable model to evaluate the role of appointment nonadherence as a covariate mediating the effects of a disparity marker (ie, African American race) on virologic failure through mediation analysis (Fig. 1 and Table 3).<sup>32–35</sup> In this final model, a shift in the parameter estimate for African American race (OR = 1.56 to 1.30) was observed, and this variable became statistically nonsignificant ( $P > 0.05$ ). Appointment nonadherence (OR = 1.78 per 25% MVP, 95% CI = 1.48 to 2.13) was significantly associated with virologic failure. The estimate of the association between African American race and virologic failure was reduced by 41% (95% CI = 21% to 100%) after adjustment for appointment nonadherence. Notably, we did not identify significant interactions between MVP and any independent variables included in the multivariate model.

## DISCUSSION

Our study found that primary HIV care appointment nonadherence significantly contributes to racial disparities in HIV virologic failure. Missed outpatient HIV appointments were more common in African American patients (step 1, path a) and were associated with HIV virologic failure among patients engaged in outpatient HIV treatment (step 2, path b). Further, the magnitude of the observed relationship between African American race and virologic failure (step 3, path c) became attenuated and statistically nonsignificant with the addition of a hypothesized mediator, appointment nonadherence, to the multivariable model (step 4, path c'). Although additional factors certainly contribute, these findings suggest that interventions targeting appointment nonadherence may serve as a building block to address racial disparities in HIV virologic outcomes.

**TABLE 2.** Factors Associated With Failure to Receive ARV Therapy Among 1151 ARV Treatment-Eligible HIV Primary Care Patients at the UAB 1917 HIV/AIDS Clinic, August 2004 to January 2007

Characteristics	ARV (n = 1110)*	No ARV (n = 41)*	Crude OR (95% CI) for No ARV	Adjusted OR (95% CI) for No ARV†
Age, yrs	42.2 ± 9.2	40.1 ± 9.1	0.77 (0.55 to 1.09)‡	0.95 (0.65 to 1.37)‡
Sex				
Male	850 (76.6)	30 (73.2)	1.0	1.0
Female	260 (23.4)	11 (26.8)	1.20 (0.59 to 2.43)	1.11 (0.52 to 2.38)
Race				
White	604 (54.4)	17 (41.5)	1.0	1.0
African American	506 (45.6)	24 (58.5)	1.69 (0.90 to 3.17)	1.24 (0.60 to 2.56)
Insurance				
Private	465 (41.9)	15 (36.6)	1.0	1.0
Public	394 (35.5)	11 (26.8)	0.87 (0.39 to 1.91)	0.75 (0.33 to 1.71)
Uninsured	251 (22.6)	15 (36.6)	1.85 (0.89 to 3.85)	1.42 (0.65 to 3.13)
Affective mental health disorder				
No	555 (50.0)	22 (53.7)	1.0	1.0
Yes	555 (50.0)	19 (46.3)	0.86 (0.46 to 1.61)	1.12 (0.57 to 2.20)
Alcohol abuse				
No	977 (88.0)	34 (82.9)	1.0	1.0
Yes	133 (12.0)	7 (17.1)	1.51 (0.66 to 3.48)	1.53 (0.63 to 3.73)
Substance abuse				
No	902 (81.3)	33 (80.5)	1.0	1.0
Yes	208 (18.7)	8 (19.5)	1.05 (0.48 to 2.31)	0.85 (0.36 to 2.00)
No. total appointments	9.7 ± 3.8	8.3 ± 3.0	0.87 (0.78 to 0.97)§	0.90 (0.81 to 1.01)
MVP	20.2 ± 19.6	35.9 ± 25.6	2.27 (1.62 to 3.19)  ¶	2.03 (1.40 to 2.95)  ¶

\*Data presented as n (column percent) or mean ± SD.

†Multivariable logistic regression model controls for other variables displayed in the table. Model characteristics: Hosmer–Lemeshow goodness-of-fit statistic, *P* = 0.49, c statistic = 0.73.

‡Odds ratio for 10 years increments.

§*P* < 0.05.

||Odds ratio for 25% increments.

¶*P* < 0.01.

Although the current study highlights the role of appointment nonadherence in contributing to racial disparities in virologic failure, we are unable to determine the root causes of missed visits among African American patients. We suspect that access to ancillary services such as transportation and case management,<sup>41,42</sup> patient-provider relationships,<sup>43,44</sup> health beliefs, and distrust in the health care system may contribute.<sup>45,46</sup> Formative studies exploring the role of these and other factors will be critical to the development of interventions to improve appointment adherence in African Americans with HIV infection. Furthermore, future research should employ mediation methods to evaluate other pathways through which racial disparities in HIV outcomes occur, such that additional targets for intervention may be identified.

It has been noted that pathways mediating racial/ethnic health care disparities are likely to involve a complex interplay of health care, public health, and social factors.<sup>7</sup> Clearly, much work needs to be done to better understand the intricate processes mediating health care disparities in HIV infection and to provide confirmation of our findings and more details regarding the role of appointment nonadherence. From the health care system perspective, future studies may explore the role of differential receipt of ARV medications. Among our study sample who attended ≥4 visits over ≥6 months, no

difference in ARV receipt was observed along racial lines. However, evaluation of the all clinic patients with at least 1 visit during the study period showed that African Americans were less likely to receive ARVs when such treatment was indicated. These findings suggest the importance of retention in HIV care as it relates to racial disparities in receipt of ARV therapy.

In a landmark study, Shapiro et al<sup>2</sup> identified disparities in receipt of protease inhibitors among HIV-infected African Americans in a national probability sample of people living with HIV/AIDS, which began enrollment shortly after this class of drugs became available. Recent studies examining racial disparities in ARV receipt have yielded mixed results; some studies have identified persisting disparities, whereas others demonstrate similar ARV receipt by race/ethnicity.<sup>29,30,47</sup> It is noteworthy that most of these studies, including ours, evaluate ARV receipt using a cross-sectional design and focus on patients engaged in care. Effective treatment of HIV infection necessitates long-term, continuous treatment with ARV medications. In addition to lower receipt of ARVs among patients with more missed visits as shown in the current study, it is expected that patients with worse appointment adherence are less likely to consistently receive ARV therapy during longitudinal follow-up. We speculate that appointment

**TABLE 3.** Factors Associated With Failure to Achieve an Undetectable Plasma HIV RNA Level (VL <50 Copies/mL) Among 1088 HIV Primary Care Patients at the UAB 1917 HIV/AIDS Clinic Receiving ARV Treatment, August 2004 to January 2007, Staged Multivariable Mediation Modeling

Characteristics	VL < 50 Copies/mL (n = 640)*	VL ≥ 50 Copies/mL (n = 448)*	Crude OR (95% CI) for VL ≥ 50 Copies/mL	Adjusted OR (95% CI) for VL ≥ 50 Copies/mL†	Mediation Model Adjusted OR (95% CI) for VL ≥ 50 Copies/mL‡
Age (yrs)	43.4 ± 9.2	40.8 ± 9.1	0.73 (0.64 to 0.84) <sup>  </sup>	0.75 (0.65 to 0.87) <sup>  </sup>	0.78 (0.68 to 0.91) <sup>  </sup>
Gender					
Male	497 (77.7)	338 (75.5)	1.0	1.0	1.0
Female	143 (22.3)	110 (24.6)	1.13 (0.85 to 1.50)	0.85 (0.62 to 1.16)	0.82 (0.59 to 1.13)
Race					
White	386 (60.3)	212 (47.3)	1.0	1.0	1.0
African American	254 (39.7)	236 (52.7)	1.69 (1.33 to 2.16) <sup>§</sup>	1.56 (1.19 to 2.05) <sup>§</sup>	1.30 (0.98 to 1.72)
Insurance					
Private	312 (48.8)	144 (32.1)	1.0	1.0	1.0
Public	194 (30.3)	194 (43.3)	2.17 (1.64 to 2.87) <sup>§</sup>	1.82 (1.35 to 2.44) <sup>§</sup>	1.62 (1.20 to 2.20) <sup>§</sup>
Uninsured	134 (20.9)	110 (24.6)	1.78 (1.29 to 2.45) <sup>§</sup>	1.31 (0.93 to 1.85)	1.21 (0.86 to 1.72)
Affective mental health disorder					
No	328 (51.3)	211 (47.1)	1.0	1.0	1.0
Yes	312 (48.7)	237 (52.9)	1.18 (0.93 to 1.50)	1.15 (0.88 to 1.49)	1.18 (0.90 to 1.54)
Alcohol abuse					
No	569 (88.9)	388 (86.6)	1.0	1.0	1.0
Yes	71 (11.1)	60 (13.4)	1.24 (0.86 to 1.79)	1.05 (0.71 to 1.57)	1.00 (0.66 to 1.51)
Substance abuse					
No	542 (84.7)	343 (76.6)	1.0	1.0	1.0
Yes	98 (15.3)	105 (23.4)	1.69 (1.25 to 2.30) <sup>§</sup>	1.39 (0.99 to 1.95)	1.27 (0.90 to 1.80)
No. total appointments	9.4 ± 3.3	10.4 ± 4.3	1.08 (1.04 to 1.11) <sup>§</sup>	1.05 (1.01 to 1.09) <sup>§</sup>	1.06 (1.02 to 1.10) <sup>§</sup>
MVP	15.5 ± 16.8	24.7 ± 19.4	2.00 (1.68 to 2.38) <sup>¶</sup>	—	1.78 (1.48 to 2.13) <sup>¶</sup>

\*Data presented as n (column percent) or mean ± SD.

†Multivariable logistic regression model controls for other variables with numeric values displayed in the table. Model characteristics: Hosmer–Lemeshow goodness-of-fit statistic,  $P = 0.88$ ,  $c$  statistic = 0.65.‡Multivariable logistic regression model controls for all variables displayed in the table. Model characteristics: Hosmer–Lemeshow goodness-of-fit statistic,  $P = 0.96$ ,  $c$  statistic = 0.68.§ $P < 0.01$ .

||Odds ratio for 10 years increments.

¶Odds ratio for 25% increments.

nonadherence results in inferior HIV outcomes, as observed in this study, through less consistent receipt of ARV medications among those with missed visits and worse ARV medication adherence in these individuals.

Recently, increased attention has focused on linkage and retention to HIV clinical care.<sup>48–50</sup> This expanded focus comes at a critical juncture as the number of new patients in need of HIV care is expected to increase dramatically in the coming years in response to the revised Centers for Disease Control and Prevention HIV testing recommendations that now advocate routine opt-out HIV testing for adults in all health care settings.<sup>51–53</sup> Our study found clinic appointment adherence was worse in African Americans, younger patients, those with public health insurance, and patients with substance and alcohol abuse disorders. Previously we found that racial/ethnic minorities, females, and those lacking private health insurance were less likely to establish care at our clinic after calling to schedule an initial appointment.<sup>24</sup> Collectively, these studies highlight a sobering challenge to the HIV research, policy, and outreach communities; to identify barriers and develop

interventions to improve linkage and retention to clinical care among these underserved patient populations who bear a disproportionate burden of the US HIV epidemic.<sup>54</sup> The findings from our study suggest that such interventions may play a role in attenuating HIV health care disparities.

Specific limitations may limit interpretation of our findings. As an observational study, we are able to identify associations but cannot attribute causality. As a single center, academically affiliated HIV treatment center in the southeast United States, our findings may or may not be generalizable to other settings or patient populations. Our study included patients with 4 or more scheduled appointments occurring over 6 months or longer during the 30-month study period. As such, patients at the extreme of nonadherence, those lost to follow-up before accumulating 4 visits, are not included in these analyses. However, compared with patients included in this study, excluded patients (ie, those with <4 visits over <6 months) were more likely to be African American, younger, and lacking private insurance (data not shown); sociodemographic characteristics associated with appointment

nonadherence among study participants. This suggests that our study may actually *underestimate* the true impact of appointment nonadherence in these groups.

In summary, our study found that HIV clinic appointment adherence was worse in African Americans. Furthermore, appointment nonadherence was associated with failure to receive ARV medications and failure to achieve an undetectable HIV VL (<50 copies/mL) among patients receiving treatment. Finally, our study identifies a role of missed visits in contributing to racial disparities in virologic failure observed in African Americans. Although other factors are certainly at play on the pathway mediating racial/ethnic HIV disparities, appointment nonadherence seems to play an important role. This study highlights the need to move beyond descriptive studies of health care disparities to identify pathways that may inform interventions to address and overcome inequities for those that bear a disproportionate burden of the US HIV epidemic.

### ACKNOWLEDGMENTS

We thank the UAB 1917 Clinic Cohort management team for their assistance with this project ([www.uab1917cliniccohort.org](http://www.uab1917cliniccohort.org)).

### REFERENCES

- Levine RS, Briggs NC, Kilbourne BS, et al. Black white mortality from HIV-disease before and after introduction of HAART in 1996. *Am J Public Health*. 2007;97:1884–1892.
- Shapiro MF, Morton SC, McCaffrey DF, et al. Variations in the care of HIV-infected adults in the United States: results from the HIV Cost and Services Utilization Study. *JAMA*. 1999;281:2305–2315.
- Stone VE. Optimizing the care of minority patients with HIV/AIDS. *Clin Infect Dis*. 2004;38:400–404.
- Betancourt JR. Eliminating racial and ethnic disparities in health care: what is the role of academic medicine? *Acad Med*. 2006;81:788–792.
- Lurie N. Health disparities—less talk, more action. *N Engl J Med*. 2005;353:727–729.
- Beach MC, Gary TL, Price EG, et al. Improving health care quality for racial/ethnic minorities: a systematic review of the best evidence regarding provider and organization interventions. *BMC Public Health*. 2006;6:104.
- Lurie N, Dubowitz T. Health disparities and access to health. *JAMA*. 2007;297:1118–1121.
- Institute of Medicine of the National Academies. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare*. Washington, DC: National Academies Press; 2003.
- Andrulis DP. Access to care is the centerpiece in the elimination of socioeconomic disparities in health. *Ann Intern Med*. 1998;129:412–416.
- Eisenberg JM, Power EJ. Transforming insurance coverage into quality health care: voltage drops from potential to delivered quality. *JAMA*. 2000;284:2100–2107.
- Lasser KE, Himmelstein DU, Woolhandler S. Access to care, health status, and health disparities in the United States and Canada: results of a cross-national population-based survey. *Am J Public Health*. 2006;96:1300–1307.
- Catz SL, McClure JB, Jones GN, et al. Predictors of outpatient medical appointment attendance among persons with HIV. *AIDS Care*. 1999;11:361–373.
- Israelski D, Gore-Felton C, Power R, et al. Sociodemographic characteristics associated with medical appointment adherence among HIV-seropositive patients seeking treatment in a county outpatient facility. *Prev Med*. 2001;33:470–475.
- Kissinger P, Cohen D, Brandon W, et al. Compliance with public sector HIV medical care. *J Natl Med Assoc*. 1995;87(1):19–24.
- Palacio H, Shiboski CH, Yelin EH, et al. Access to and utilization of primary care services among HIV-infected women. *J Acquir Immune Defic Syndr*. 1999;21:293–300.
- Giordano TP, Gifford AL, Clinton WA, et al. Retention in care: a challenge to survival with HIV infection. *Clin Infect Dis*. 2007;44:1493–1499.
- Giordano TP, White AC Jr, Sajja P, et al. Factors associated with the use of highly active antiretroviral therapy in patients newly entering care in an urban clinic. *J Acquir Immune Defic Syndr*. 2003;32:399–405.
- Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. *Ann Intern Med*. 1999;131:81–87.
- Park WB, Choe PG, Kim SH, et al. One-year adherence to clinic visits after highly active antiretroviral therapy: a predictor of clinical progress in HIV patients. *J Intern Med*. 2007;261:268–275.
- Rastegar DA, Fingerhood MI, Jasinski DR. Highly active antiretroviral therapy outcomes in a primary care clinic. *AIDS Care*. 2003;15:231–237.
- Robbins GK, Daniels B, Zheng H, et al. Predictors of antiretroviral treatment failure in an urban HIV clinic. *J Acquir Immune Defic Syndr*. 2007;44:30–37.
- Valdez H, Lederman MM, Woolley I, et al. Human immunodeficiency virus 1 protease inhibitors in clinical practice: predictors of virological outcome. *Arch Intern Med*. 1999;159:1771–1776.
- Chen RY, Accortt NA, Westfall AO, et al. Distribution of health care expenditures for HIV-infected patients. *Clin Infect Dis*. 2006;42:1003–1010.
- Mugavero MJ, Lin HY, Allison JJ, et al. Failure to establish HIV care: characterizing the “no show” phenomenon. *Clin Infect Dis*. 2007;45:127–130.
- Willig JH, Westfall AO, Allison J, et al. Nucleoside reverse-transcriptase inhibitor dosing errors in an outpatient HIV clinic in the electronic medical record era. *Clin Infect Dis*. 2007;45:658–661.
- Keruly JC, Conviser R, Moore RD. Association of medical insurance and other factors with receipt of antiretroviral therapy. *Am J Public Health*. 2002;92:852–857.
- Melnikow J, Kiefe C. Patient compliance and medical research: issues in methodology. *J Gen Intern Med*. 1994;9:96–105.
- Cohen MH, Cook JA, Grey D, et al. Medically eligible women who do not use HAART: the importance of abuse, drug use, and race. *Am J Public Health*. 2004;94:1147–1151.
- Gebo KA, Fleishman JA, Conviser R, et al. Racial and gender disparities in receipt of highly active antiretroviral therapy persist in a multistate sample of HIV patients in 2001. *J Acquir Immune Defic Syndr*. 2005;38:96–103.
- Pence BW, Ostermann J, Kumar V, et al. Use, duration, and success of antiretroviral therapy: the influence of psychosocial characteristics and race/ethnicity. *J Acquir Immune Defic Syndr*. 2008;47:194–201.
- Hammer SM, Saag MS, Schechter M, et al. Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society—USA panel. *JAMA*. 2006;296:827–843.
- Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol*. 1986;51:1173–1182.
- Bryan A, Schmiede SJ, Broaddus MR. Mediation analysis in HIV/AIDS research: estimating multivariate path analytic models in a structural equation modeling framework. *AIDS Behav*. 2007;11:365–383.
- MacKinnon DP. Analysis of mediating variables in prevention and intervention research. *NIDA Res Monogr*. 1994;139:127–153.
- MacKinnon DP, Fairchild AJ, Fritz MS. Mediation analysis. *Annu Rev Psychol*. 2007;58:593–614.
- Cole SR, Hernan MA. Fallibility in estimating direct effects. *Int J Epidemiol*. 2002;31:163–165.
- Robins JM, Greenland S. Identifiability and exchangeability for direct and indirect effects. *Epidemiology*. 1992;3:143–155.
- Kaufman JS, Maclehorse RF, Kaufman S. A further critique of the analytic strategy of adjusting for covariates to identify biologic mediation. *Epidemiol Perspect Innov*. 2004;1:4.
- Bodnar LM, Ness RB, Harger GF, et al. Inflammation and triglycerides partially mediate the effect of prepregnancy body mass index on the risk of preeclampsia. *Am J Epidemiol*. 2005;162:1198–1206.
- Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol Methods*. 2002;7:422–445.

41. Conviser R, Pounds MB. Background for the studies on ancillary services and primary care use. *AIDS Care*. 2002;14(Suppl 1):S7–S14.
42. Katz MH, Cunningham WE, Fleishman JA, et al. Effect of case management on unmet needs and utilization of medical care and medications among HIV-infected persons. *Ann Intern Med*. 2001;135(8 Pt 1):557–565.
43. Schneider J, Kaplan SH, Greenfield S, et al. Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection. *J Gen Intern Med*. 2004;19:1096–1103.
44. Beach MC, Keruly J, Moore RD. Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *J Gen Intern Med*. 2006;21:661–665.
45. Whetten K, Leserman J, Whetten R, et al. Exploring lack of trust in care providers and the government as a barrier to health service use. *Am J Public Health*. 2006;96:716–721.
46. Bogart LM, Thorburn S. Are HIV/AIDS conspiracy beliefs a barrier to HIV prevention among African Americans? *J Acquir Immune Defic Syndr*. 2005;38:213–218.
47. Palacio H, Kahn JG, Richards TA, et al. Effect of race and/or ethnicity in use of antiretrovirals and prophylaxis for opportunistic infection: a review of the literature. *Public Health Rep*. 2002;117:233–251. Discussion 231–232.
48. Cheever LW. Engaging HIV-infected patients in care: their lives depend on it. *Clin Infect Dis*. 2007;44:1500–1502.
49. Gardner LI, Metsch LR, Anderson-Mahoney P, et al. Efficacy of a brief case management intervention to link recently diagnosed HIV-infected persons to care. *AIDS*. 2005;19:423–431.
50. Tobias C, Cunningham WE, Cunningham CO, et al. Making the connection: the importance of engagement and retention in HIV medical care. *AIDS Patient Care STDS*. 2007;21(Suppl 1):S3–S8.
51. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep*. 2006;55(RR-14):1–17, Quiz CE11–14.
52. Mugavero MJ, Saag MS. HIV care at a crossroads: the emerging crisis in the US HIV epidemic. *MedGenMed*. 2007;9:58.
53. Saag MS. Which policy to ADAP-T: waiting lists or waiting lines? *Clin Infect Dis*. 2006;43:1365–1367.
54. Centers for Disease Control and Prevention. *HIV/AIDS Surveillance Report, 2004*. Vol 16. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2005. Also available at: <http://www.cdc.gov/hiv/stats/haslink.htm>. Accessed May 1, 2008.