Understanding the Disparity: Predictors of Virologic Failure in Women Using Highly Active Antiretroviral Therapy Vary by Race and/or Ethnicity

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Background: Stark racial/ethnic disparities in health outcomes exist among those living with HIV in the United States. One of 3 primary goals of the National HIV/AIDS Strategy is to reduce HIV-related disparities and health inequities.

Methods: Using data from HIV-infected women participating in the Women's Interagency HIV Study from April 2006 to March 2011, we measured virologic failure (HIV RNA >200 copies/mL) after suppression (HIV RNA < 80 copies/mL) on highly active antiretroviral therapy. We identified predictors of virologic failure using discrete time survival analysis and calculated racial/ethnic-specific population-attributable fractions (PAFs).

Results: Of 887 eligible women, 408 (46%) experienced virologic failure during the study period. Hispanic and white women had significantly lower hazards of virologic failure than African American women [Hispanic hazard ratio, (HR) = 0.8, 95% confidence interval: (0.6 to 0.9); white HR = 0.7 (0.5 to 0.9)]. The PAF of virologic failure associated with low income was higher in Hispanic [adjusted hazard ratios (aHR) = 2.2 (0.7 to 6.5), PAF = 49%] and African American women [aHR = 1.8 (1.1 to 3.2), PAF = 38%] than among white women [aHR = 1.4 (0.6 to 3.4), PAF = 16%]. Lack of health insurance compared with public health insurance was associated with virologic failure only among Hispanic [aHR = 2.0 (0.9 to 4.6), PAF = 22%] and white women [aHR = 1.9 (0.7 to 5.1), PAF = 13%]. By contrast, depressive symptoms were associated with virologic failure only among African-American women [aHR = 1.6 (1.2 to 2.2), PAF = 17%].

Conclusions: In this population of treated HIV-infected women, virologic failure was common, and correlates of virologic failure varied by race/ethnicity. Strategies to reduce disparities in HIV treatment outcomes by race/ethnicity should address racial/ethnic-specific barriers including depression and low income to sustain virologic suppression.

Key Words: disparities, race/ethnicity, virologic failure, HAART, HIV, women

(*J Acquir Immune Defic Syndr* 2013;64:289–298)

Received for publication March 11, 2013; accepted June 12, 2013.

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The Women's Intragency HIV Study (WIHS) is funded by the National Institute of Allergy and Infectious Diseases (UO1-AI-35004, UO1-AI-31834, UO1-AI-34994, UO1-AI-34989, UO1-AI-34993, and UO1-AI-42590) and by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (UO1-HD-32632). The study is co-funded by the National Cancer Institute, the National Institute on Drug Abuse, and the National Institute on Deafness and Other Communication Disorders. Funding is also provided by the National Center for Research Resources (UCSF-CTSI grant number UL1 RR024131).

Presented at third Annual CFAR Joint Symposium on HIV Research in Women, September 20, 2012, Providence, RI.

The authors have no conflicts of interest to disclose.

The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

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INTRODUCTION

A dramatic decrease in HIV/AIDS-related mortality and morbidity has followed the widespread introduction of highly active antiretroviral therapy (HAART) in the United States.[1,2] However, these improvements have not been equally distributed. In 2009, HIV was the fourth leading cause of death for black women 25–44 years of age.[3] In contrast, HIV was the 15th leading cause among white women 25–44 years of age the same year.[3] Women and African Americans with HIV are less likely to receive antiretroviral therapy when clinically indicated.[4–6] Among those on antiretroviral therapy, women and racial/ethnic minorities are more likely to discontinue antiretroviral therapy; and racial/ethnic minorities experience virologic failure at higher rates.[7] Most sobering, HIV-infected African Americans have higher mortality rates than HIV-infected whites overall.[8–10]

The National HIV/AIDS Strategy has 3 primary goals, 1 of which is to reduce HIV-related disparities and health inequities by addressing "the factors that influence disparate health outcomes" and being "mindful of the diversity and needs of the most affected communities".[11] African American

and Hispanic women are subject to the confluence of being both racial/ethnic minorities and female, putting them at greater risk for negative HIV-related health outcomes. HIV-infected minority women also differ in terms of behaviors, health care utilization and access, and socioeconomic status from HIV-infected men and whites; thereby making it critical to investigate the specific barriers these women experience in achieving optimal health outcomes.

Sustained suppression of viral load is a central health outcome among HIV-infected individuals because it (1) translates to reduced morbidity and mortality in HIV-infected individuals; and (2) reduces the risk of transmitting the virus to others.[12–15] Moreover, a specific target of the National Strategy is to increase the proportion of blacks and Latinos with undetectable viral loads.[11] Prior research in the Women's Interagency HIV Study (WIHS) has shown that minority women are at higher risk for virologic failure after initial suppression on HAART.[16] Race/ethnicity has been found to be significantly associated with therapy adherence,[17] and there is substantial evidence that suboptimal adherence is highly associated with virologic failure.[16–20] Therefore, racial/ethnic disparities seen in virologic outcomes may be a function of differential adherence and investigating the factors that influence adherence among minority groups would be the next step in understanding the dynamics of the disparity.

To address the National HIV/AIDS Strategy's goal of improving population-level virologic outcomes among minorities, we examined racial/ethnic disparities in virologic failure using a broad public health approach to investigate factors associated with failure. The objective of this study was 2-fold as follows: (1) to describe the pattern of virologic failure by race/ethnicity from 2006 to 2011 in a representative cohort of HIV-infected women; and (2) to determine behavioral, psychosocial, socioeconomic, and health care–related correlates of virologic failure among HIV-infected women using HAART in an effort to inform programs that will assist in reaching the goals of the National HIV/AIDS Strategy.

METHODS

Study Population

The WIHS is an ongoing, multicenter, prospective cohort study with enrollment initially in 1994–1995 and again in 2001–2002. The initial study objective was to investigate the natural history of HIV-1 infection in adult women in the United States. The WIHS has 6 study sites located in Washington, DC; Brooklyn, NY; Bronx, NY; San Francisco, CA; Los Angeles, CA; and Chicago, IL. Detailed information on study methodology and inclusion/exclusion criteria for enrollees has been described elsewhere.[21,22] Briefly, WIHS participants attend semiannual study visits, during which they participate in structured interviews and undergo physical examinations, and provide biologic specimens for analyses and storage in repositories. Informed consent was obtained from all participants, and institutional review boards at all collaborating institutions approved study protocols.

For this analysis, a nested cohort of WIHS HIV-infected women using HAART was examined between April 1, 2006 (corresponding to the start of WIHS visit 24) and March 31, 2011 (end of visit 33). HAART was defined according to the Department of Health and Human Services guidelines as the use of 3 or more antiretroviral medications, with either a protease inhibitor, nonnucleoside reverse transcriptase inhibitor, or integrase inhibitor, usually in combination with 2 nucleoside (or nucleotide) reverse transcriptase inhibitors.[23] To best represent the population of HIV-infected women using HAART, inclusion criteria included women enrolled in the WIHS who were using HAART and were virologically suppressed at visit 23 (ie, the visit before the start of the study period, between October 1, 2005, and March 31, 2006) and women who initiated or resumed HAART after visit 23 and became virologically suppressed within 1 year of HAART initiation or resumption. Virologic suppression was defined as HIV RNA <80 copies per milliliter, and participants entered this analysis only after completing 1 visit after initial viral suppression. For our findings on racial disparities to have clear implications, women were excluded if they self-reported a racial/ethnic identity other than African American or black, Hispanic (of any race), and white.

Outcome of Interest

The outcome of interest was virologic failure after confirmed suppression (<80 copies/mL) on HAART and was defined as a viral load of ≥ 200 copies per milliliter, similar to the definition used in Department of Health and Human Services treatment guidelines.[23] Because there is no consensus on the clinical implications of transiently detectable viral loads of up to <200 copies per milliliter, women whose viral loads remained <200 copies per milliliter after suppression were not considered to experience virologic failure.[23] After virologic suppression was confirmed, HIV viral load was used as a biological surrogate for adherence to, and use of, HAART and was assessed at every semiannual visit. From April 2006 through March 2009, HIV RNA was measured using the Nuclisens HIV-1 QT assay and from April 2009 to March 2011, using the Roche Ultrasensitive assay.

Exposures of Interest

For this analysis, we were most interested in factors that may contribute to racial/ethnic disparities in virologic failure, specifically socioeconomic, psychosocial, behavioral, and health care–related factors. Factors were selected based on the review of the literature on correlates of medication adherence and virologic failure, with those that were chosen hypothesized to be related to race/ethnicity. Race/ethnicity was categorized as non-Hispanic African American or Black, Hispanic, and non–Hispanic white based on participants' self-report at WIHS enrollment. Socioeconomic covariates included educational attainment and country of birth assessed at WIHS enrollment. Annual household income was assessed annually via self-report. Depressive symptoms were assessed at each visit using a Center for Epidemiologic Studies Depression scale (CES-D)[24] score of 16 or greater. Using an adapted version of the IV Patient-Assessed Report of Status and Experience (HIV-PARSE) questionnaire,[25] a quality of life index,[26] health

perception, and cognitive function score were measured annually with a range from 0 (poor) to 100 (excellent) and scaled to a 10-point change.

Behavioral covariates measured at each visit include number of sex partners since last visit, recent drug use, current smoking status, and weekly alcohol use. Self-reported sexual identity and mode of HIV transmission were assessed at WIHS enrollment. Hepatitis C infection was assessed using antibody and RNA tests and was dichotomized here as a positive history (antibody positive or RNA positive) or no history (antibody and RNA negative).

Health care–related covariates focused on insurance coverage. Health insurance status was assessed at every visit via self-report and categorized as public (including Medicaid, Medicare, CHAMPUS/other veteran's insurance), private or other, and no health insurance. Change in health insurance coverage was also assessed by comparing coverage between 2 consecutive visits and categorized as no change, change from no health insurance to any health insurance, and change from any health insurance to no health insurance. AIDS Drug Assistance Program (ADAP) participation was assessed at each visit, regardless of health insurance coverage.

Adherence to HAART was assessed at each visit and is self-reported as the percentage of time the medications were taken as prescribed in the previous 6 months, categorized as 100%, 99%–95%, 94%–75%, less than 75% of the time, or have not taken any.

Multivariable analyses were adjusted for the following a priori hypothesized confounders: CD4 T-lymphocyte cell count (CD4 count) per cubic millimeter measured using standard flow cytometry technique[21] and lagged from the previous study visit; history of self-reported clinical AIDS diagnosis (other than CD4 count <200 cells/mm^3); time since HAART initiation; virologic failure (≥ 200 copies/mL) occurring after HAART initiation in the modern era (since 2000) and prior to the start of the study period; study site; and age. Previous virologic failure was assessed at entry into our nested study; all other confounders were measured at each visit.

Statistical Methods

Distributions of study variables were compared using Pearson χ^2 tests and Wilcoxon rank sum tests for categorical and continuous variables, respectively. To investigate the annual proportion of women experiencing virologic failure, a series of annual cross-sectional studies was conducted. A woman contributed information regarding potential failure to every calendar year in which she attended a visit after viral suppression. Trends in the annual proportion of women with virologic failure were determined using generalized linear models with generalized estimating equations using a log link with binomially distributed variance. Trends over time were assessed for the entire study population and stratified by race/ethnicity.

Predictors of virologic failure were identified using discrete time complementary log–log survival models to estimate univariate hazard ratio (HR) and adjusted hazard ratio (aHR) and their associated 95% confidence intervals. The time origin was visit 23 (October 2005 to March 2006) and the time metric was visits since visit 23. Because women could not be at risk for failure at the origin per exclusion criteria, time at risk began at visit 24. Women who initiated or resumed HAART after visit 23 and suppressed within 1 year of initiating or resuming HAART were considered late entries. These women entered the study at their visit after suppression. If a woman missed a study visit, she was not considered at risk for failure and was not included in the risk set for that visit. Women exited the study at the time of virologic failure (event) or censored at loss to follow-up, death, or administratively at the end of follow-up. Covariates and confounders measured only at enrollment into the WIHS or at the start of the study period were considered time-fixed; those measured annually or semiannually were treated as time varying.

Multivarible models were constructed for all participants and stratified by race/ethnicity. Population-attributable fractions (PAFs) were calculated for predictors from the stratified models as an estimate of the proportion of virologic failures that were associated with each risk factor, thereby highlighting women in whom the virologic failure burden is concentrated according to race/ethnicity. PAFs convey both the magnitude of the risk and the prevalence of the predictor, making it a useful metric for prioritizing and targeting subpopulations and interventions. The adjusted PAF formula as described by Rockhill et al[27] was used to appropriately estimate the PAF using adjusted hazard ratios. Analyses were conducted using Stata, version 12 (StataCorp, College Station, TX). Predictors were considered statistically significant at $P < 0.05$.

RESULTS

Participant Characteristics

Of 1483 active HAART users, 887 women met inclusion criteria over the study period, the majority (n = 614, 69%) of whom were HAART users with a suppressed viral load at the study start date. Other participants were women who initiated (n = 78, 9%) or resumed (n = 195, 22%) HAART after the study start date and achieved a suppressed viral load. A total of 4854 person-visits were included, with a median of 5 visits (interquartile range: 2–9 visits) per individual. Participants were predominantly African American (54%) and born in the United States. (76%); 37% had less than a high school education (Table 1). At entry into our nested study, 71% had an average annual household income of $\leq$\$24,000, 60% were unemployed, and 63% had public health insurance.

Of the 887 women, 408 (46%) experienced virologic failure from April 2006 to March 2011. The median number of study visits completed before failure was 3 (IQR: 1–4) and median viral load at failure was 3.3 $\log_{10}$ copies per milliliter. Women who experienced virologic failure were more likely to be African American, United States native, younger, have a lower household annual income, use alcohol, cigarettes, and illicit drugs, hold public health insurance, have a lower CD4 count, and previously experience a virologic failure (Table 1). At the visit in which women experienced failure, 93%

TABLE 1. Characteristics of WIHS participants by virologic failure, April 2006 to March 2011 (n = 887)

	Suppressed		Virologic Failure			Total	
	n = 479		n = 408			n = 887	
Characteristic	**n**	**%**	**n**	**%**	***P****	**n**	**%**
Characteristics measured at enrollment into the WIHS							
Race/ethnicity							
Non-Hispanic African American	240	50.1	241	59.1	0.015	481	54.2
Hispanic	150	31.3	114	27.9		264	29.8
Non-Hispanic White and other	89	18.6	53	13.0		142	16.0
Educational attainment							
Less than high school	172	35.9	160	39.2	0.210	332	37.4
High school diploma	126	26.3	117	28.7		243	27.4
More than high school	181	37.8	131	32.1		312	35.2
Country of birth							
United States and territories	344	71.8	332	81.4	0.001	676	76.2
Other	134	28.0	76	18.6		210	23.7
Mode of HIV transmission							
Intravenous drug use	97	20.3	91	22.3	0.279	188	21.2
Heterosexual contact	203	42.4	183	44.9		386	43.5
Transfusion	14	2.9	5	1.2		19	2.1
None identified	159	33.2	129	31.6		288	32.5
History of hepatitis C infection							
No	345	72.0	279	68.4	0.231	624	70.3
Yes	126	26.3	122	29.9		248	28.0
Characteristics measured at entry into our nested study							
Age (yrs), median (IQR)	45.1 (38.6–50.9)		43.2 (37.1–49.6)		0.004	44.1 (38.2–50.3)	
Average annual household income							
≤$24,000	305	63.7	294	72.1	0.003	599	67.5
$24,001–$36,000	52	10.9	50	12.3		102	11.5
≥$36,001	97	20.3	49	12.0		146	16.5
Marital status							
Married or living with partner	172	35.9	122	29.9	0.049	294	33.1
Widowed, divorced/annulled, separated, other	161	33.6	143	35.0		304	34.3
Never married	120	25.0	130	31.9		250	28.2
Residence							
Own home	420	87.7	355	87.0	0.727	775	87.4
Not own home	55	11.5	50	12.3		105	11.8
Currently employed							
No	277	57.8	255	62.5	0.160	532	60.0
Yes	198	41.3	150	36.8		348	39.2
Depressive symptoms							
No	311	64.9	247	60.5	0.162	558	62.9
Yes	158	33.0	153	37.5		311	35.1
Drug use since last study visit†							
No	412	86.0	321	78.7	0.004	733	82.6
Yes	62	12.9	82	20.0		144	16.2
Alcohol use since last study visit							
<3 drinks/week	445	92.9	354	86.8	0.002	799	90.1
≥3 drinks/week	29	6.1	49	12.0		78	8.8
Type of health insurance‡							
Public	270	56.4	280	68.6	<0.001	550	62.0
Private or other	122	25.5	65	15.9		187	21.1
No insurance	82	17.1	58	14.2		140	15.8
Current cigarette smoker							
No	338	70.6	228	55.9	<0.001	566	63.8
Yes	136	28.4	175	42.9		311	35.1

TABLE 1. (*Continued*) Characteristics of WIHS participants by virologic failure, April 2006 to March 2011 (n = 887)

	Suppressed		Virologic Failure			Total	
	n = 479		n = 408			n = 887	
Characteristic	**n**	**%**	**n**	**%**	***P****	**n**	**%**
CD4 count (cells/mm^3), median (IQR)	541 (395–731)		450 (311–672)		<0.001	505 (353–700)	
Clinical AIDS diagnosis							
No	291	60.8	233	57.1	0.271	524	59.1
Yes	188	39.2	175	42.9		363	40.9
Years since HAART initiation (median/IQR)	8.2 (5.4–9.4)		8.2 (5.4–9.3)		0.608	8.2 (5.4–9.4)	
Previous virological failure (viral load ≥ 200 copies/mL) since HAART initiation in recent HAART era							
No	147	30.7	58	14.2	<0.001	205	23.1
Yes	278	58.0	316	77.5		594	67.0

Percentages may not add to 100% due to missing data.
* χ^2 test for categorical variables and Wilcoxon rank sum test for continuous variables.
† Any drug use defined to be marijuana, crack, cocaine, heroin, illicit methadone, methamphetamines, or any other illicit drug.
‡ Public = Medicaid, Medicare, Medi-CAL, Veterans; Private; and other includes student health insurance.
IQR, interquartile range.

reported HAART use and 67% reported 95% or higher adherence to their antiretroviral medications.

Pattern of Virologic Failure

The annual proportion of women experiencing virologic failure remained stable over the study period (*P* value for trend = 0.483, Fig. 1). The annual proportion of failure from 2007 to 2010 among all women ranged from 23% to 27%. African American women consistently had a higher annual proportion of failure as compared with Hispanic and white women. The absolute mean difference between African American and Hispanic women was 5% and between African American and white women was 11%.

Predictors of Virologic Failure

Hispanic and white women had a significantly lower risk of virologic failure compared with African American women in univariate analysis [HR = 0.75 (0.60 to 0.94) and HR = 0.65 (0.48 to 0.87), respectively, Table 2]. Of the 887 study participants, 768 (87%) had complete data for all the covariates and were included in the multivariable analyses. After adjustment for other potential predictors and confounders, race/ethnicity was no longer associated with virologic failure (Hispanic vs. African American aHR = 0.99 (0.76 to 1.32); White vs. African American aHR = 0.80 (0.56, 1.12)]. Birth within the United States, low annual household income (≤$24,000), depressive symptoms, alcohol use, current smoking, and ADAP nonparticipation were

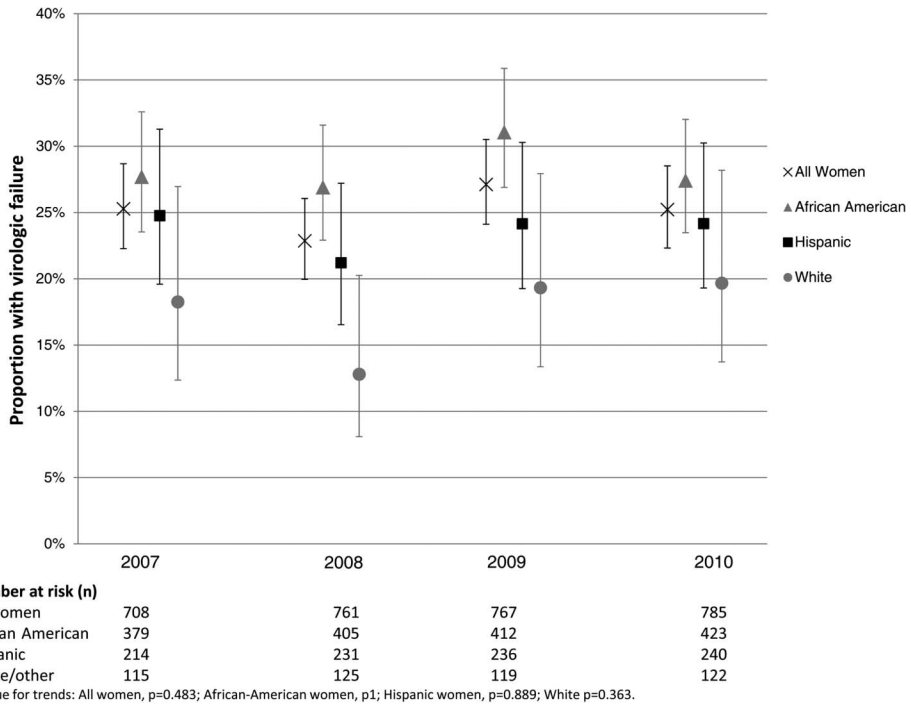

FIGURE 1. Annual proportion (and 95% confidence intervals) of women with virologic failure, by race/ethnicity, the WIHS, 2007–2010. The *P* value for trends: All women, *P* = 0.483; African American women, *P* = 1; Hispanic women, *P* = 0.889; white, *P* = 0.363.

TABLE 2. Univariate and adjusted hazard ratios (HR and aHR, respectively) of virologic failure, WIHS, April 2006 to March 2011 (n = 768)

Predictor	Univariate Analysis HR (95% CI)	Multivariable Analysis aHR* (95% CI)
Socioeconomic factors		
Race/ethnicity		
Non-Hispanic African American	Reference	Reference
Hispanic	**0.75 (0.60 to 0.94)**	0.99 (0.76 to 1.32)
Non-Hispanic white and other	**0.65 (0.48 to 0.87)**	0.80 (0.56 to 1.12)
Educational attainment		
Less than high school	Reference	—
High school diploma	0.98 (0.77 to 1.24)	—
More than high school	0.86 (0.67 to 1.09)	—
Country of birth		
United States and territories	**1.63 (1.27 to 2.09)**	**1.67 (1.17 to 2.40)**
Other	Reference	Reference
Average annual household income		
≤$24,000	**1.75 (1.30 to 2.36)**	**1.80 (1.19 to 2.72)**
$24,001-$36,000	1.31 (0.88 to 1.97)	1.41 (0.90 to 2.23)
≥$36,001	Reference	Reference
Psychosocial factors		
Depressive symptoms		
No	Reference	Reference
Yes	**1.64 (1.35 to 2.00)**	**1.32 (1.06 to 1.66)**
Quality of life score (per 10 points)	**0.95 (0.90 to 0.99)**	—
Health perception score (per 10 points)	**0.95 (0.91 to 0.99)**	—
Cognitive function score (per 10 points)	**0.95 (0.91 to 0.99)**	—
Behavioral factors		
Sexual identity		
Heterosexual/straight	Reference	—
Bisexual and other	1.26 (0.85 to 1.88)	—
Lesbian/gay	1.43 (0.87 to 2.37)	—
Had one or more sexual partners since last study visit		
No	Reference	—
Yes	1.06 (0.87 to 1.30)	—
Mode of HIV transmission		
Intravenous drug use	Reference	—
Heterosexual contact	0.85 (0.66 to 1.09)	—
Transfusion	0.41 (0.17 to 1.02)	—
None identified	0.81 (0.62 to 1.06)	—
Drug use since last study visit†		
No	Reference	Reference
Yes	**1.58 (1.23 to 2.03)**	0.98 (0.72 to 1.33)
Alcohol use since last study visit		
<3 drinks/week	Reference	Reference
≥3 drinks/week	**1.80 (1.35 to 2.40)**	**1.53 (1.08 to 2.18)**
History of hepatitis C infection		
No	Reference	Reference
Yes	**1.26 (1.02 to 1.55)**	1.28 (0.99, 1.66)
Current cigarette smoker		
No	Reference	Reference
Yes	**1.83 (1.50 to 2.23)**	**1.38 (1.09 to 1.74)**
Health care-related factors		
Type of health insurance‡		
Public	Reference	Reference
Private or other	**0.63 (0.48 to 0.82)**	1.20 (0.82 to 1.76)
No insurance	**0.71 (0.54 to 0.94)**	1.46 (0.98 to 2.16)
Change in health insurance coverage since last study visit		
No change	Reference	Reference
No health insurance to any health insurance	0.93 (0.54 to 1.62)	—
Any health insurance to no health insurance	1.13 (0.70 to 1.81)	—
Currently have ADAP		
No	**1.45 (1.14 to 1.85)**	**1.41 (1.02 to 1.94)**
Yes	Reference	Reference

Bolded results indicate statistical significance at the *P* value of 0.05 level.

* Adjusted for all other predictors in the model and study center, age, CD4 count, clinical AIDS diagnosis, time since HAART initiation, and previous virologic failure.

† Any drug use defined to be marijuana, crack, cocaine, heroin, illicit methadone, methamphetamines, or any other illicit drug.

‡ Public = Medicaid, Medicare, Medi-CAL, Veterans; Private and other includes student health insurance.

CI, confidence interval.

significantly associated with an increased risk of failure after adjustment.

Predictors by Race/Ethnicity

Adjusted stratified analyses examined predictors of virologic failure separately for the 3 racial/ethnic groups. Birth within the United States, annual income ≤$24,000, depressive symptoms, and current smoking were associated with significantly higher hazard of failure among African American women (n = 406) (Fig. 2). No predictors reached statistical significance for Hispanic and white women, likely due to loss of precision from small sample size; therefore, the magnitude and direction of point estimates were compared across racial/ethnic groups. Among Hispanic (n = 240) and white women (n = 122), an increase in hazard with low income was evident. Hispanic women who recently used drugs had a higher risk of virologic failure, but this was not seen among African American or white women. Compared with women with public health insurance, those with no health insurance had about a 2-fold increase in the risk of failure among Hispanic and white women. African American women without health insurance did not have an increased risk of failure. Similar to African American women, Hispanic and white women without ADAP demonstrated the suggestion of higher risk of failure. Among white women, those reporting 3 or more alcoholic drinks per week had an almost 2-fold higher risk of virologic failure compared with those reporting less than 3 drinks per week, which was not seen in African American or Hispanic women. In contrast to Hispanic

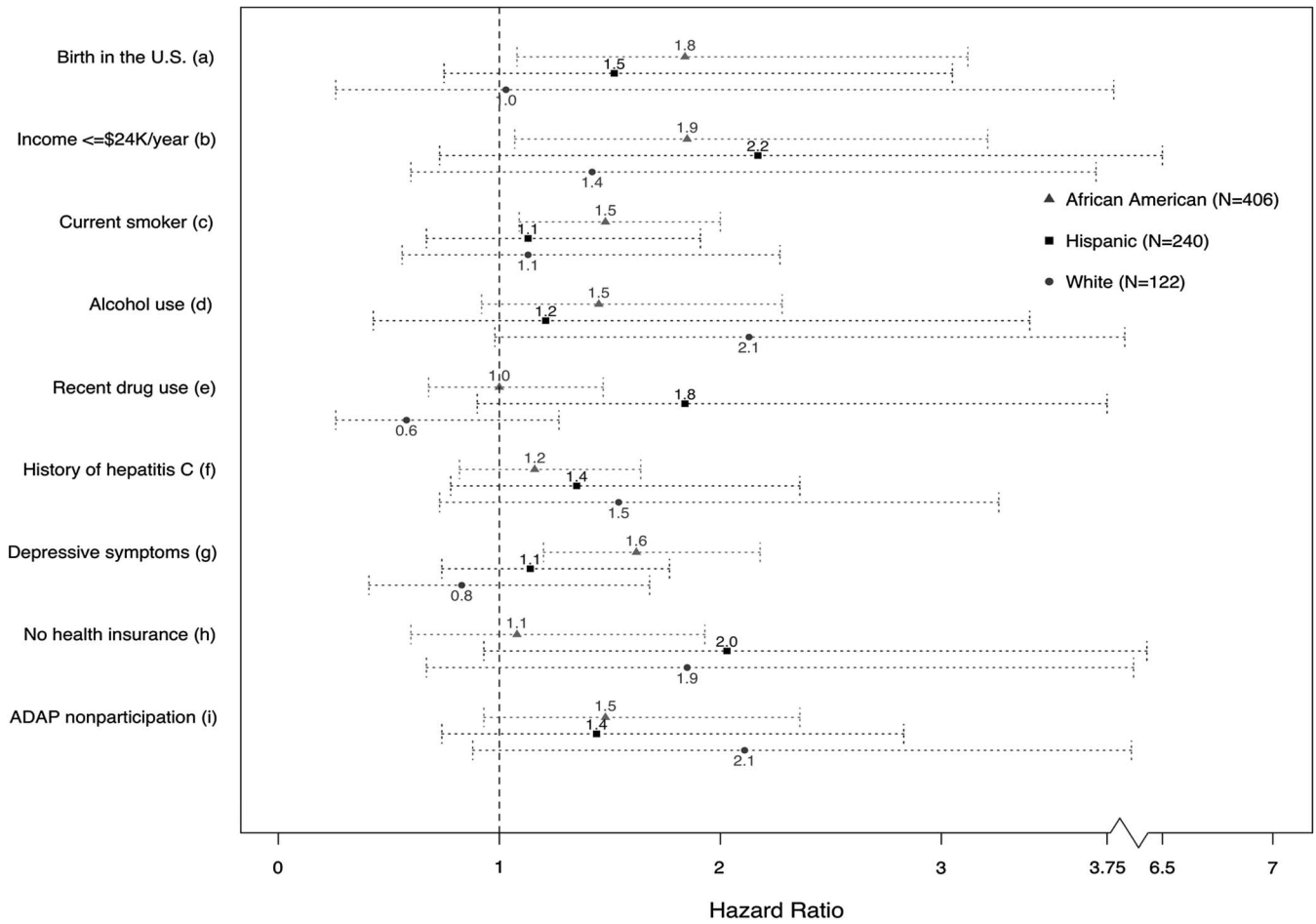

FIGURE 2. The aHR* of virologic failure by race/ethnicity, WIHS, April 2006 to March 2011 (n = 768). *Adjusted for all predictors in the figure and study center, age, CD4 count, clinical AIDS diagnosis, time since HAART initiation, and previous virologic failure. [a]Compared with other country of birth; [b]Compared with annual income ≥$36,001; [c]Compared with nonsmoker, [d]≥3 drinks per week compared with <3 drinks per week; [e]Compared with nonuse; [f]Compared with no history of hepatitis C; [g]Compared with no depressive symptoms; [h]Compared with public health insurance; [i]Compared with ADAP participation.

and African American women, depressive symptoms and recent drug use suggested a lower risk of failure in white women.

Race/Ethnicity-Specific Population Attributable Fractions

PAFs were calculated for each racial/ethnic-specific group using the aHRs from the stratified multivariable models and the prevalence that experienced virologic failure by predictor. ADAP nonparticipation had high PAFs in all 3 racial/ethnic groups, with an especially large PAF among white women (Fig. 3). The PAF associated with low annual income and native birth was considerably higher in African American (38% and 41%) and Hispanic women (49% and 20%) than in white women (16% and 3%). Among African American women, the PAFs for depressive symptoms (17%) and current smoking (16%) were high compared with those of Hispanic and white women. The PAF associated with a lack of health insurance was higher in white (13%) and Hispanic (22%) women, although negligible in African American women.

DISCUSSION

Reducing HIV-related disparities and health inequities plays a prominent role in the National HIV/AIDS Strategy[11]; in the era of treatment as prevention, strategies to support adherence to HAART and maintenance of suppressed viral load are critical.[28–30] In this representative population of HIV-infected women using HAART, virologic failure was very common, nearly half experienced failure over the 5-year study period. Predictors associated with the risk of virologic failure differed by racial/ethnic group, and the PAFs highlight that specific predictors contribute differently to the burden of failure across racial/ethnic groups. This suggests that a 1-size-fits-all approach to virologic failure may not be appropriate for this treated population.

Each year, approximately 25% of study participants experienced virologic failure even though 68% of these women self-reported at least 95% adherence to HAART, demonstrating substantial misclassification in self-reported adherence. African American women consistently had a higher probability of failure compared with Hispanic and

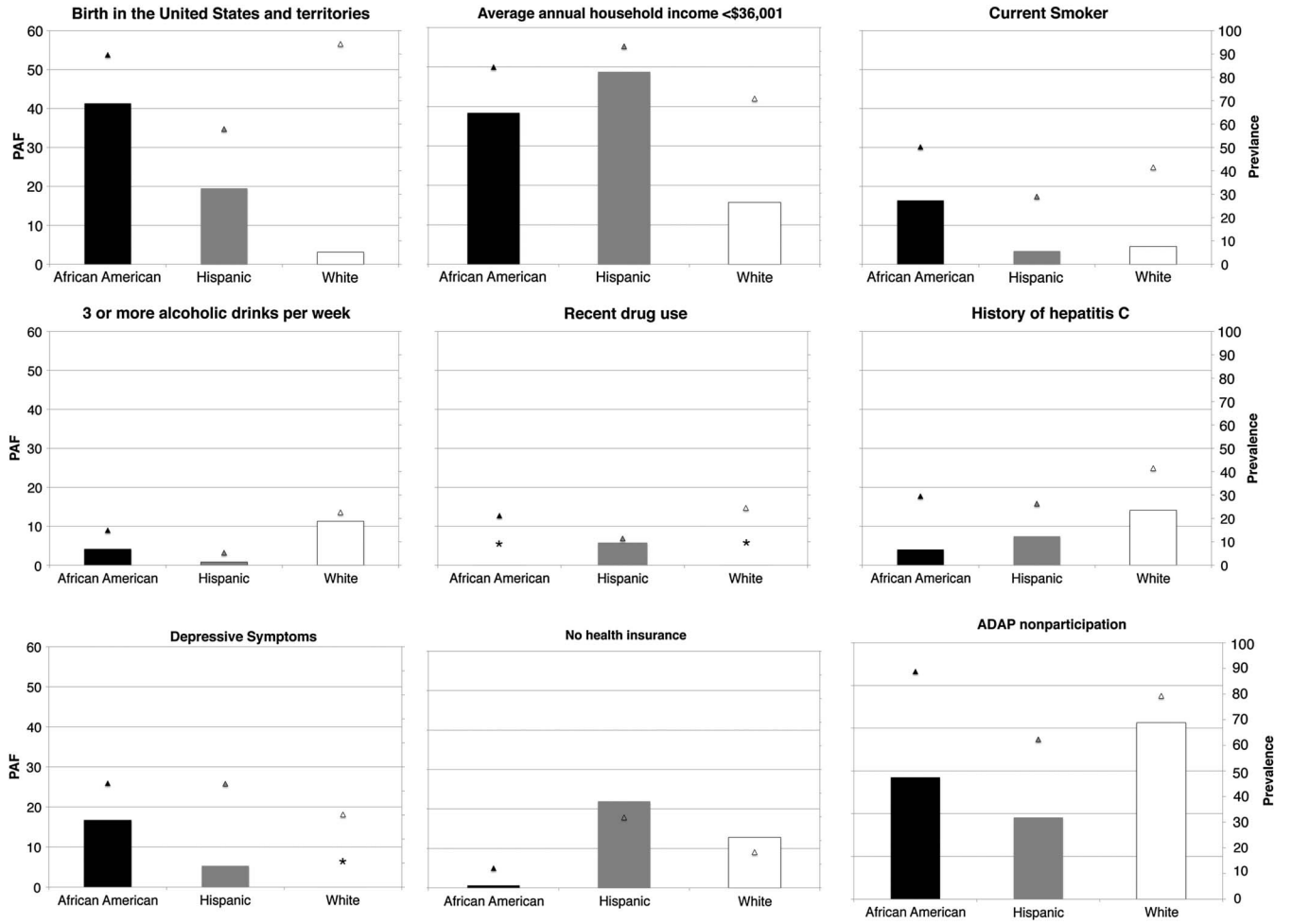

FIGURE 3. PAF and prevalence of predictors stratified by race/ethnicity, WIHS, April 2006 to March 2011 (n = 792). Bars represent PAF; Triangles represent prevalence; *Negative population attributable fraction.

white women. This analysis extends the previous WIHS study on racial/ethnic disparities in virologic failure[16] to the current era. Our findings corroborate multiple studies showing that racial/ethnic minorities continue to have poorer HIV-related health outcomes[31] and add to the literature by suggesting differential causes of failure by racial/ethnic group.

As expected, race/ethnicity was strongly associated with virologic failure, but this association was attenuated after adjustment for socioeconomic, behavioral, and other factors. We did not envision self-reported race/ethnicity as a genetic or biological construct but rather reflective of the socioeconomic, behavioral, historical, and contextual (eg, access to care) backgrounds experienced by different racial/ethnic groups in the modern United States. The lack of association between race/ethnicity and virologic failure after adjustment for these factors suggests that these factors play critical roles in explaining the racial/ethnic disparity in virologic failure.

Overall, the study findings highlight that several predictors of failure are persistent across racial/ethnic groups, although others vary by race/ethnicity. The aHRs and PAFs in the stratified analysis suggest that low income may be a large barrier to sustained virologic suppression for all racial/ethnic groups, though there is greater burden among Hispanic and African American women. Across all groups, there was a similar trend of increased risk of virologic failure with nonparticipation in ADAP. A previous study in the WIHS from Illinois, California, and New York found that women without ADAP were more than 2 times as likely to not currently be using HAART.[32] This study therefore extends this previous finding to a major consequence of nonuse of HAART, namely virologic failure. This finding is important given current nationwide budget reductions in ADAP funding. Birth within United States demonstrated an increased risk in virologic failure and a high PAF among African American and Hispanic women. This likely reflects differences in background and resources between immigrants and native US participants. For example, among HIV-infected immigrants, adherence to HAART and staying healthy may fulfill a social responsibility, and becoming sick may carry serious financial consequences.

Depressive symptoms were significantly associated with virologic failure with a correspondingly high PAF only among African American women. Other previous studies have reported depression to be associated with decreased adherence to therapy,[33–35] HAART nonuse and discontinuation,[16,36] and

AIDS-related death.[37] Our findings highlight that depression may be a large contributor of decreased adherence to, or cessation of HAART, leading to virologic failure in African American women but not among other racial/ethnic groups. This finding could be related to racial/ethnic differences in social support, coping, and self-efficacy. Current smoking was significantly associated with an increased hazard of virologic failure and was highly prevalent in American American women, resulting in a moderately high PAF. Previous studies have provided evidence that smoking may interfere with the pharmacodynamics of HAART and be a strong indicator for women at-risk for suboptimal adherence, discontinuation of therapy, and eventually, virologic failure.[38,39] Hispanic and white women had twice the hazard of failure if they lacked health insurance compared with having public health insurance; this finding was notably absent from African American women. Insurance coverage has previously been linked to use and receipt of antiretroviral therapy,[16,40,41] and our findings suggest that lack of health insurance coverage remains a considerable barrier to continued virologic suppression, although less among African American women.

Although we adjusted for virologic failure before the start of the study period, analyses that consider multiple failures may provide further information that is applicable and relevant to public health interventions. Our survival analysis investigated only the first episode of virologic failure within the study period rather than all instances of failure. For patients with high viral load measurements, repeat viral load tests are often conducted. However, in the WIHS, viral load is measured only once at each semiannual study visit, limiting our ability to confirm the high viral load. Also limiting were the small sample sizes resulting from stratification by race/ethnicity, likely decreasing the power to discern significant predictors among Hispanic and white women. Despite these limitations, our article is among the first to examine drivers of racial/ethnic disparities in virologic failure by looking at predictors and PAFs stratified by racial/ethnic group. Importantly, our use of the PAF was not intended as a measure of causal potential, as the interpretation of the PAF requires a causal relationship, but rather an estimate of the total burden associated with each factor.

In conclusion, this analysis highlights the women at greatest risk for virologic failure in a representative US-based cohort and informs interventions to decrease racial/ethnic disparities. Understanding drivers of these disparities may prove vital in planning and implementing targeted interventions for different populations and reducing mortality and morbidity in the majority of women with HIV. Such knowledge also provides information regarding next steps to ultimately reach the National HIV Strategy goals by reducing racial/ethnic disparities in virologic failure.

ACKNOWLEDGMENTS

Data in this article were collected by the WIHS Collaborative Study Group with centers (Principal Investigators) at New York City/Bronx Consortium (Kathryn Anastos); Brooklyn, NY (Howard Minkoff); Washington DC, Metropolitan Consortium (Mary Young); The Connie Wofsy Study Consortium of Northern California (Ruth Greenblatt); Los Angeles County/Southern California Consortium (Alexandra Levine); Chicago Consortium (Mardge Cohen); Data Coordinating Center (Stephen Gange).

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