Poster # 560

Impact of Race on the Response to Highly-Active Antiretroviral Therapy The Women's Interagency HIV Study

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ABSTRACT UPDATED

Context: The occurrence of AIDS defining illness (ADI) and death, and longitudinal changes in HIV-1 RNA and CD4+ cell counts following initiation of highly active antiretroviral therapy (HAART) among different racial groups have not been well described

Objective: To determine the association of race and other socio-demographic variables with response to HAART in HIV-1 infected women.

Design, participants: Prospective cohort study

Study population: 937 HIV-1 infected participants in the Women's Interagency HIV Study initiating HAART between July 1, 1995 and September 30, 2002.

Results: Over a median 4.3 years, in univariate Cox regression analyses, white women were more likely than African American women to experience virologic response (RH=1.32, p=0.010) and less likely to experience virologic rebound (RH=0.74, p=0.048). Hispanic women were less likely than African American women to develop a new ADI (RH=0.73, p=0.024) and to die (RH=0.54, p=0.010). In multivariate analyses including demographic and clinical variables associated with poorer response (discontinuation of HAART, depression, income and current drug use) there were no significant differences (p>0.05) by race in any outcome.

Conclusion: In this study of nearly 1000 women initiating HAART in the United States, after adjustment for depression, continuation of HAART, income, adherence and current drug use, there were no significant differences by race in virologic, immunologic or clinical outcomes.

INTRODUCTION

The efficacy of antiretroviral therapies has been studied predominately in men of European descent. Concern has been raised that differences in biologically determined pathways of drug metabolism and transport, which vary by race, may impact unfavorably on response to HAART in groups other than white men. Contributing to these concerns is the observation that although highly active antiretroviral therapy (HAART) has markedly improved the prognosis of HIV-1 infected individuals, improvements in outcomes have not equally benefited all demographic groups. In the United States, white men have experienced an 80% decline in mortality, compared to 50% and 65% declines in black women and men, respectively, from 1995 through 2001 (1). Although some of this variation may result from differential access to HAART (2), the contribution of other factors is not known.

CONCLUSIONS

In univariate analyses:

White women were more likely than African American women to experience virologic and immunologic response, and less likely to experience virologic rebound.

Hispanic women were more likely than African American women to experience immunologic failure, less likely to report an incident ADI, and less likely to die from any cause, but not from AIDS

After adjustment for discontinuation of HAART, depression and current drug use, and adherence, there were **no significant differences by race** in virologic, immunologic or clinical responses to HAART

Continuous use of HAART was the strongest predictor of favorable virologic, immunologic and clinical responses, with a 15-fold increased likelihood of virologic response, and a 2/3 decreased likelihood of experiencing virologic or immunologic failure, or death from AIDS

Depression was associated with a poorer virologic response, increased likelihood of immunologic rebound, and higher rate of all cause death.

Lower self reported adherence was associated with poorer virologic and immunologic response, and greater likelihood of virologic failure

Our results suggest that sociodemographic factors continue to have an adverse effect on African American women with HIV-infection. Remedies for these differences should be sought

In many outcomes, including death from AIDS, and virologic and immunologic response, there were 15-22% non-significant differences by race, with African American women doing more poorly. Longer follow up of this and other cohorts is important to determine if such differences, which would have clinical significance, are real.

METHODS

Objective

To assess the impact of race on response to HAART, with adjustment for sociodemographic factors, continuation of HAART once initiated, and adherence.

Measurements

HIV-1 RNA, CD4+ cell counts, incident AIDS defining illness (ADI), death

Study Population

937 HIV-1 infected participants in the Women's Interagency HIV Study who initiated HAART between July 1995 and September 2002, had a HAART initiation date known within 1 year, were followed up after HAART initiation, and whose self classified race was Black, white, or hispanic. The women's Interagency HIV Study is a prospective, multi-site cohort study of natural and treated history in 2,068 HIV-1 infected women in the United States.

Primary Outcome Variables and definitions

a. Virologic response: the first time HIV-1 RNA < 80 cps/ml

b. Virologic rebound: the first time HIV-1 RNA > 1000 cps/ml after virologic response

c. Immunologic response: the first time CD4+ lymphocyte counts were at least 100 cells greater than nadir pre-HAART CD4+ levels

d. Immunologic failure: the first time CD4+ lymphocyte counts were below nadir pre-HAART level **after** immunologic response

e. Incident new AIDS defining illness (ADI)

f. Death, all cause, and **AIDS deaths** occurring through September 2002.

Primary Exposure Variable

Race, based on self-categorization and defined as:

a. African-American (Hispanic and non-Hispanic)

b. white (Hispanic and non-Hispanic), and

c. Hispanic (women identifying as Hispanic but neither African-American nor white). Thus, women who reported being African-American and Hispanic were classified as African-American, and white women who also reported being Hispanic were classified as white.

Secondary Exposure Variable

Educational attainment at study entry, AIDS defining illness reported prior to HAART initiation, self reported adherence after October 1998, and time dependent HAART continuation, income, depression and drug use.

Statistical Methods

Univariate and multivariate relative hazards and 95% confidence intervals, were obtained through Cox proportional hazards models using fixed (race, education), and time dependent covariates (HAART use, income, depression).

RESULTS

Table 1: Demographic and baseline (prior to HAART initiation) clinical characteristics of the 937 included women

Table 1. Characteristics of Women Initiating HAART (Values in bold if p-value < 0.10)

	African-American (n=557)	White (n=179)	Hispanic (n=201)	p-value
Median Date of HAART initiation	**September 1997**	**January 1997**	**April 1997**	**<0.001**
Age at last Pre-HAART visit Median (IQR)	**40.2 (34.4, 45.1)**	**38.0 (34.0, 42.0)**	**37.0 (32.6, 41.5)**	**<0.001**
Pre-HAART peak HIV-1 RNA Median (IQR)	84000 (23000, 250000)	80000 (19000, 300000)	78000 (19000, 250000)	0.761
Pre-HAART Nadir CD4 Median (IQR)	197 (91, 324)	214 (91, 330)	220 (102, 345)	0.419
% with Pre-HAART AIDS	47.4	42.5	44.3	0.457
% with Hepatitis C	44.9	40.4	38.0	0.203
% ART Naive prior to HAART initiation	10.8	11.7	12.4	0.800
Baseline Risk Category				
% IDU	**32.9**	**35.4**	**28.6**	**0.009**
% Heterosexual risk	**42.3**	**50.0**	**40.7**	
% Transfusion risk	**5.1**	**3.4**	**3.5**	
% None	**19.7**	**11.2**	**27.1**	
Reporting any drug use* at last pre-HAART visit (%)	**19.5**	**10.7**	**8.6**	**<0.001**
Depressed at last pre-HAART visit (%)	**50.6**	**42.2**	**57.1**	**0.021**
Smoking at last pre-HAART visit (%)	**60.9**	**46.9**	**38.1**	**<0.001**
Income < $12000 at last pre-HAART visit (%)	**64.3**	**36.5**	**70.4**	**<0.001**
Not completing high school at study entry (%)	**34.4**	**15.3**	**55.3**	**<0.001**
Reporting ≥95% adherence** to therapy at HAART initiation (%)	73.5	79.3	72.1	0.704
Remained on HAART or ART after HAART initiation (%)	**59.3**	**79.3**	**48.3**	**<0.001**

* any drug use defined to be cocaine, heroine, or crack
** data after October 1998 for a total 274 participants: 185 African-American women, 46 white women, and 43 Hispanic women

Table 2: Results of Univariate Cox Regression Analyses of virologic, immunologic and clinical outcomes after HAART initiation Values in **bold** if p-value <0.10

Race/Ethnicity	% with event	RH* (95% CI**)	p-value
	Virologic Response after HAART Initiation		
African-American	56.7% (316/557)	1.0	--
White	68.7% (123/179)	**1.32** (1.07, 1.62)	**0.010**
Hispanic	61.2% (123/201)	1.08 (0.87, 1.32)	0.498
	Virologic Rebound after Virologic Response		
African-American	62.9% (180/286)	1.0	--
White	52.3% (56/107)	**0.74** (0.55, 1.00)	**0.048**
Hispanic	65.5% (76/116)	1.06 (0.81, 1.38)	0.691
	Immunologic Response after HAART Initiation		
African-American	76.5% (426/557)	1.0	--
White	80.5% (144/179)	**1.19** (0.99, 1.44)	**0.068**
Hispanic	73.6% (148/201)	0.90 (0.74, 1.08)	0.248
	Immunologic Failure after Immunologic Response		
African-American	33.3% (135/405)	1.0	--
White	28.7% (39/136)	**0.74** (0.52, 1.06)	**0.097**
Hispanic	47.1% (66/140)	**1.44** (1.07, 1.93)	**0.016**
	Incident ADI after HAART Initiation		
African-American	39.7% (212/534)	1.0	--
White	36.3% (61/168)	0.82 (0.62, 1.09)	0.179
Hispanic	33.5% (65/194)	**0.73** (0.55, 0.96)	**0.024**
	Death after HAART Initiation		
African-American	17.6% (98/557)	1.0	--
White	11.7% (21/179)	**0.65** (0.40, 1.04)	**0.069**
Hispanic	10.5% (21/201)	**0.54** (0.34, 0.86)	**0.010**
	Death from AIDS after HAART Initiation		
African-American	6.5% (36/557)	1.0	
White	3.4% (6/179)	0.52	0.141
Hispanic	5.5% (11/201)	0.80	0.515

*RH = relative hazard
**CI = confidence interval

Table 3. Univariate and Bivariate Analyses of the association of adherence measured as a time-dependent covariate with laboratory and clinical outcomes after HAART initiation (RH = relative hazard)

Values in **bold** if p-value <0.10

	Virologic Response		Virologic Failure		Immunologic Response		Immunologic Failure		Incident ADI		Death		AIDS Death	
	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value
Adherence*														
Univariate	**2.28**	**<0.001**	**0.34**	**<0.001**	**1.48**	**0.007**	**0.71**	**0.091**	**0.68**	**0.019**	0.72	0.221	**0.40**	**0.080**
Bivariate with race/ethnicity	**2.26**	**<0.001**	**0.35**	**<0.001**	**1.48**	**0.007**	**0.71**	**0.093**	**0.68**	**0.018**	0.75	0.299	**0.42**	**0.098**
Race (bivariate with adherence)														
African American	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--
White	1.18	0.280	0.76	0.177	0.96	0.789	0.82	0.465	1.03	0.885	0.61	0.100	UND*	--
Hispanic	0.96	0.817	0.94	0.758	0.77	0.130	**1.86**	**0.002**	0.86	0.441	0.88	0.675	2.07	0.172

ation adherence data available for 848 participants who contributed 4586 semester-visits a
ombination or HAART reported; of these women, AIDS death occurred in 15 women, of wh
nic. Therefore RH for white women could not be determined.

Table 4: Multivariate Analyses of laboratory and clinical outcomes after HAART Initiation (RH = relative hazard)

Values in **bold** if p-value <0.10

	Virologic Response		Virologic Failure		Immunologic Response		Immunologic Failure		Incident ADI		Death		AIDS Death	
	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value	RH	p-value
[illegible]														
African-American	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--
White	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Hispanic	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]														
No therapy	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--	1.0	--
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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*Also adjusted for self-reported baseline HIV-1 exposure category, current drug use, income; all p-values >0.10 except current drug use with AIDS death (RH=2.57, p=0.015)

ACKNOWLEDGEMENTS

Data in this manuscript were collected by the Women's Interagency HIV Study (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, Phyllis Tien); Los Angeles County/Southern California Consortium (Alexandra Levine); Chicago Consortium (Mardge Cohen); Data Coordinating Center (Alvaro Muñoz). The WIHS is funded by the National Institute of Allergy and Infectious Diseases, with contributions from the National Cancer Institute, the National Institute of Child Health & Human Development, The National Institute on Drug Abuse, the National Institute of Dental and Craniofacial Research.