Racial Differences in Response to Antiretroviral Therapy for HIV Infection: An AIDS Clinical Trials Group (ACTG) Study Analysis

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Background. In the United States, black individuals infected with human immunodeficiency virus (HIV) have higher rates of virologic failure on antiretroviral therapy (ART) and of death compared to white individuals. The cause for these disparities is uncertain. We sought to examine differences in virologic outcomes among antiretroviral-naive clinical trial participants starting randomized ART and to investigate factors to explain the differences.

Methods. Individual-level data from participants initiating ART in 5 AIDS Clinical Trials Group studies were analyzed. Included studies were those conducted during 1998–2006 with a primary outcome of virologic failure. The primary outcome measure was time to virologic failure, regardless of ART changes.

Results. A total of 2495 individuals (1151 black; 1344 white) were included with a median follow-up of 129 weeks. Compared to whites, blacks had an increased hazard of virologic failure (hazard ratio [HR]; 1.7; 95% confidence interval [CI], 1.4–1.9; *P* < .001), with no evidence of heterogeneity across regimens (*P* = .97); the association remained after adjustment for measured confounders (HR, 1.4; 95% CI, 1.2–1.6; *P* < .001). Increased hazard of virologic failure was associated with younger age, higher pretreatment HIV type 1 RNA level, lower pretreatment CD4 cell count, hepatitis C antibody, less education, and recent nonadherence to treatment. Sensitivity analyses with different endpoint definitions demonstrated similar results.

Conclusions. In this analysis, blacks had a 40% higher virologic failure risk than whites that was not explained by measured confounders. The observation was consistent over a range of regimens, suggesting that the difference may be driven by social factors; however, biological factors cannot be ruled out. Further research should identify the sources of racial disparities and develop strategies to reduce them.

Keywords. HIV-1; antiretroviral therapy; racial disparity; virologic failure.

Racial differences in human immunodeficiency virus (HIV)/AIDS in the United States are well recognized,

with nearly half of all new HIV diagnoses occurring among black individuals and an HIV prevalence rate 8-fold higher in blacks compared to whites [1]. The prognosis of HIV infection also is poorer for blacks in the United States, with a 9-fold higher death rate compared to whites. These racial disparities are thought to be multifactorial; possible factors include demographic, clinical, socioeconomic, and other reasons, such as access to and quality of healthcare, individual behaviors, and attitudes, including the level of trust in the healthcare system [2–4].

Data regarding responses to antiretroviral treatment (ART) are varied. Among 435 patients from the

southern United States, minority racial/ethnic groups (mostly black) were more likely to discontinue ART earlier and experience virologic failure compared to whites [5]. Other studies have shown similar differences but suggested they may be explained by pretreatment characteristics, medication adherence, and access to care [6–9]. Two reports from settings with ready access to healthcare described persistent differences in virologic responses between minority racial/ethnic groups and whites [10–11], whereas a recent large study found that black race was not associated with decreased virologic responses, but psychosocial factors and place of residence were [12].

Racial/ethnic differences in ART responses in several AIDS Clinical Trials Group (ACTG) studies were previously examined on a study-by-study basis [13–15]. In the current analysis, data from large randomized ACTG studies of ART-naive participants in which virologic outcome was the primary endpoint were combined to examine differences in efficacy between black and white participants and the extent to which these differences can be explained by measured confounders. Randomized assignment to ART in these studies removes the important confounder of access to ART that can affect assessment of race-based outcomes. Given access to all individual-level data, ART outcomes could be examined in an identical way.

METHODS

Study Population
Our study included ART-naive individuals who self-identified as non-Hispanic black or white who initiated randomized ART in 5 ACTG clinical trials conducted between 1998 and 2006 (ACTG 384 [16, 17], ACTG 388 [18], A5073 [19], A5095 [20], and A5142 [21]), with a primary endpoint including virologic failure. We excluded individuals who self-identified as Hispanic (n = 645) due to significant differences in the ART regimens used between men and women; other races (n = 97) due to insufficient numbers; and individuals who never initiated randomized ART. We also excluded individuals randomized to directly observed therapy as part of study A5073 [22] and those randomized to an inferior regimen of 3 nucleoside reverse transcriptase inhibitors (NRTIs) from study A5095 [23].

The ART regimens studied included 2 or 3 NRTIs with a nonnucleoside reverse transcriptase inhibitor (NNRTI); 2 NRTIs with 1–2 protease inhibitors (PIs) with or without ritonavir boosting (PI/r or PI); an NNRTI with PI/r; or a triple-class regimen including 2 NRTIs, an NNRTI, and an unboosted PI (Supplementary Table 1). Study evaluations and antiretroviral drugs were supplied at no cost to participants, with the exception that some medications were not supplied in study A5142 (Supplementary Table 1); however, study eligibility required assurance that access to these drugs was readily available. Participants underwent clinical assessments at least every 8 weeks, including HIV type 1 (HIV-1) RNA levels and CD4 cell count determinations. Self-reported ART adherence and socioeconomic measures were captured using a standardized questionnaire [24] in a subset of individuals (92% and 46%, respectively; Supplementary Table 1). Studies were approved by participating sites' institutional review boards; all participants provided written informed consent. The Supplementary Data include tabular summaries of key design features of the 5 trials as well as definitions and modeling considerations of potential confounding factors.

Study Endpoints
The primary endpoint of the analysis was the time to virologic failure determined regardless of changes in ART (intention-to-treat), defined as the time from study entry to the first of 2 consecutive HIV-1 RNA levels >1000 copies/mL, with the first at or after study week 16 and before study week 24, or >200 copies/mL with the first at or after study week 24. Failure was determined by a single measurement if this was the last sample collected. For study discontinuation prior to week 16, individuals with an HIV-1 RNA level <0.5 $\log_{10}$ lower than baseline and >50 copies/mL at week 4 or <1 $\log_{10}$ lower than baseline and >50 copies/mL at week 8 also were considered virologic failures. All remaining participants had virologic failure time censored at the time of the last measured HIV-1 RNA level.

Secondary endpoints included as-treated virologic failure, where individuals were censored at discontinuation of randomized ART (not including within-class drug substitutions); a combined endpoint of the first of virologic failure or discontinuation of randomized ART (regimen completion); CD4 cell count changes from baseline; and study drug adherence (Supplementary Table 2). As sensitivity analyses, analyses were repeated excluding participants randomized to regimens containing unboosted PIs (including triple-class regimens) and limited to those with full data available for the socioeconomic variables of interest.

Statistical Considerations
Pretreatment characteristics and socioeconomic factors were compared between groups using Wilcoxon rank-sum tests and χ^2 tests as appropriate. Failure-time distributions were estimated using Kaplan-Meier methods and compared with log-rank tests. The association of race on the hazard of virologic failure (intention-to-treat and as-treated) and regimen completion was estimated using Cox proportional hazards models stratified by study and ART regimen. Multivariable analysis considered the following factors assessed pretreatment: age, HIV-1 RNA level, CD4 cell count, hepatitis C antibody, self-reported mode of HIV infection, highest education level, Center for Epidemiologic Studies Depression Scale score [25], number of children in

household, self-efficacy, perceived social support, perception of ART, alcohol use, and marijuana use. Self-reported medication adherence over the prior 4 days was assessed at approximate 8-week intervals. Specific details of covariate definitions are provided in Supplementary Table 2.

Final model selection used a forward stepwise approach, retaining covariates significant at $P < .1$. In the event of substantial missing/unavailable categorical data, an "unknown" category was included to retain the overall sample size. Interactions of race with all covariates in the final adjusted model were evaluated sequentially. Proportional hazards were evaluated for all final model covariates sequentially by inclusion of interactions with the natural logarithm of time. In the event of evidence suggesting violation of proportional hazards, the violating covariate was reparameterized to allow for estimation of a time-varying hazard (over the first 6-months, at 6–12 months, and after 1 year).

Differences in CD4 cell count change from baseline were evaluated using Wilcoxon rank-sum tests, linear regression was used to adjust for potential confounding, and failure-time analyses were used to consider the time to CD4 increase ≥ 250 cells/μL. Ordered categories of self-reported adherence were compared by race using generalized estimating equations [26].

All analyses used SAS software version 9.2 (SAS Institute Inc, Cary, NC). Access to all individual-level study data was available for analysis.

RESULTS

Between 1998 and 2006, 2556 black or white ART-naive individuals were enrolled in 1 of the 5 ACTG studies and 2495 were included in our analysis; 16 who did not start randomized ART and 45 not followed after entry were excluded. ART regimens included NRTI + NNRTI (41%), NRTI + PI (19%), NRTI + PI/r (16%), NNRTI + PI/r (8%), and a triple-class (NRTI + NNRTI + PI) regimen (17%). Median follow-up was 129 weeks and was similarly distributed by race; 43% of participants had >3 years of follow-up (Table 1).

The population was 46% black and 54% white, 19% female and 81% male, with a median age of 37 years, baseline HIV-1 RNA 100 000 copies/mL, and baseline CD4 count 210 cells/μL. At baseline compared to whites, blacks were more likely to be female, to have lower pretreatment HIV-1 RNA levels and CD4 cell counts, and to have hepatitis C antibody (all $P < .001$). White men were most likely to report education beyond high school ($P < .001$); women of both races reported lower education than

Table 1. Characteristics and Follow-up of the Study Population

Characteristic	Total (n = 2495)	Male White[a] (n = 1202)	Male Black[a] (n = 820)	Female White[a] (n = 142)	Female Black[a] (n = 331)	P Value
Trial characteristics						
Treatment-naive study						
ACTG 384	776 (31%)	399 (33%)	237 (29%)	48 (34%)	92 (28%)	<.001
ACTG 388	362 (15%)	197 (16%)	107 (13%)	26 (18%)	32 (10%)	
A5073	200 (8%)	88 (7%)	72 (9%)	7 (5%)	33 (10%)	
A5095	573 (23%)	271 (23%)	196 (24%)	36 (25%)	70 (21%)	
A5142	584 (23%)	247 (21%)	208 (25%)	25 (18%)	104 (31%)	
Randomized ART regimen class						
NNRTI-based[b]	1012 (41%)	491 (41%)	340 (41%)	55 (39%)	126 (38%)	<.001
PI/r-based[b]	403 (16%)	170 (14%)	143 (17%)	13 (9%)	77 (23%)	
PI-based[b]	479 (19%)	249 (21%)	140 (17%)	36 (25%)	54 (16%)	
PI/r + NNRTI	188 (8%)	75 (6%)	74 (9%)	11 (8%)	28 (8%)	
Triple-class	413 (17%)	217 (18%)	123 (15%)	27 (19%)	46 (14%)	
Duration of follow-up, wk, median (Q1-Q3)	129 (89–168)	131 (97–161)	129 (75–154)	129 (95–155)	125 (66–152)	. . .
Patient characteristics						
Age, y, median	37	37	38	39	36	.31
HIV-1 RNA level, $\log_{10}$ copies/mL, median (Q1–Q3)	5.0 (4.5–5.5)	5.1 (4.6–5.6)	4.9 (4.4–5.5)	4.9 (4.3–5.5)	4.7 (4.2–5.3)	<.001
CD4 count[c], cells/μL, median (Q1–Q3)	210 (65–355)	244 (81–391)	178 (37–311)	209 (81–354)	199 (78–326)	<.001
Ever hepatitis C antibody positive[d]	11%	8%	16%	12%	10%	<.001

Table 1 continued.

Characteristic	Total (n = 2495)	Male White[a] (n = 1202)	Male Black[a] (n = 820)	Female White[a] (n = 142)	Female Black[a] (n = 331)	P Value
Self-reported demographics (% with data)[e]	1142 (46%)	585 (49%)	352 (43%)	65 (46%)	140 (42%)	
Mode of HIV infection[f]						
Shared needles	8%	6%	10%	17%	8%	<.001
Sexual contact	82%	87%	75%	74%	82%	
Needle stick/transfusion	2%	2%	2%	5%	2%	
Highest education level						
Less than high school graduate	13%	7%	17%	16%	23%	<.001
High school graduate	30%	27%	31%	38%	40%	
Some college	32%	32%	35%	26%	30%	
Bachelor's degree	16%	21%	12%	14%	6%	
Postgraduate	8%	13%	5%	5%	1%	
Self-efficacy						
Not at all/somewhat sure	10%	9%	12%	14%	15%	.22
Very sure	31%	31%	30%	35%	35%	
Extremely sure	58%	61%	58%	51%	51%	
Perception that ART will have a positive effect on health						
Not at all/somewhat sure	28%	24%	34%	23%	27%	<.001
Very sure	36%	38%	30%	43%	40%	
Extremely sure	36%	38%	35%	34%	33%	
Perceived social support						
Very/somewhat dissatisfied	12%	10%	12%	11%	16%	.54
Somewhat satisfied	29%	28%	31%	34%	29%	
Very satisfied	58%	61%	57%	55%	55%	
Alcohol use[g]						
≤20 drinks per month	41%	45%	35%	45%	34%	<.001
>20 drinks per month	22%	27%	20%	16%	8%	
Marijuana use[h]						
Yes	41%	44%	42%	27%	24%	.007

Data are presented as No. (%) unless otherwise specified. *P* values are given for test of general differences across the 4 subgroups using a Wilcoxon rank-sum test for continuous outcomes and χ^2 test for categorical outcomes. Percentages are taken of the total race/sex cohort.

Abbreviations: ACTG, AIDS Clinical Trials Group; ART, antiretroviral therapy; HIV-1, human immunodeficiency virus type 1; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PI/r, PI taken with low-dose ritonavir for pharmacological boosting; Q1, 1st quartile (25th percentile); Q3,3rd quartile (75th percentile).

[a] Individuals of self-identified Hispanic ethnicity are excluded.

[b] Taken in combination with 2–3 nucleoside reverse transcriptase inhibitors.

[c] Pretreatment CD4 cell count was missing for 3 subjects.

[d] Due to serology not collected by study at study entry, 675 individuals had unknown hepatitis C exposure status.

[e] Percentage of individuals with data for at least 1 self-report measure (excluding highest education level). With the exception of highest level of education, self-report data were captured only in a subset of participants of ACTG 388 and ACTG 384 and all participants in A5073; data were not collected in A5095 and A5142. Education status was available for a larger proportion of the study population (n = 2033 [81%]) through their participation in ACTG 5001, a rollover study designed for long-term follow-up [39]. Additional details regarding questioning for self-report outcomes are provided in Supplementary Table 2.

[f] Not shown; the remaining 8% of participants completing a questionnaire responded "Do not know."

[g] Not shown; the remaining 38% of participants completing a questionnaire reported never drinking.

[h] Marijuana use in the past 6 months.

men (Table 1). Although self-reported medication adherence in the cohort was high, whites reported fewer missed doses of medication compared to blacks across all metrics ($P \le .001$). For a metric defined as the number of days reporting at least 1 missed dose, the proportion of blacks reporting in each category (1, 2, 3, or 4 days) was higher compared to whites (Figure 1).

A total of 854 participants (468 black, 386 white) met criteria for virologic failure. The time to virologic failure was significantly
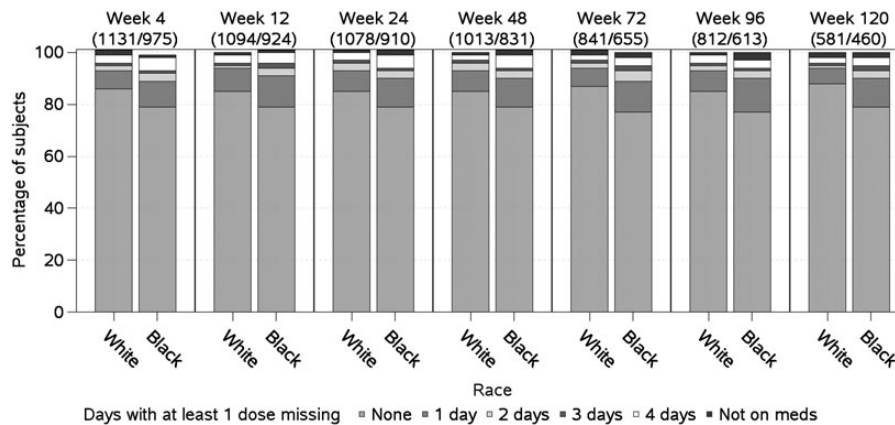
Figure 1. Self-reported adherence over time. Percentage of subjects reporting 0, 1, 2, 3, or 4 days with at least 1 dose missed over a 4-day recall period by study week. Longitudinal self-reported adherence data were only captured for a subset (92%) of individuals; the numbers of subjects contributing data by study week are given for white/black race, respectively.

shorter for blacks compared to whites ($P < .001$); the 3-year cumulative probability of virologic failure was 45% (95% confidence interval [CI], 42%–48%) for blacks compared to 32% (95% CI, 29%–35%) for whites (Figure 2*A*). Virologic failure-time distributions were not different by sex ($P = .72$; Figure 2*B*) or race/sex combined ($P = .81$; Figure 2*C*). There were differences in failure-time distributions according to ART regimen class; specifically, higher rates of virologic failure were observed for subjects randomized to nonboosted PIs ($P < .001$; Figure 2*D*).

In unadjusted Cox proportional hazards analysis stratified by ART and study, compared to white race, black race was associated with increased hazard of virologic failure (hazard ratio [HR], 1.7 [95% CI, 1.4–1.9], $P < .001$) without evidence of heterogeneity across the 15 ART regimens ($P = .97$; Figure 3*A*). A significant association of black race remained apparent (HR, 1.4 [95% CI, 1.2–1.6], $P < .001$) following adjustment for measured confounders. Factors also associated with increased hazard of virologic failure in adjusted analyses included younger age, higher pretreatment HIV-1 RNA level, lower pretreatment CD4 cell count, hepatitis C antibody positivity, less education, and recent nonadherence. Of these, all but age and HIV-1 RNA level were more common among blacks (Figure 3*B*).

Although lower self-reported satisfaction with support and lower perception that ART would have a positive effect on health were significantly associated with an increased hazard of virologic failure in unadjusted analyses, these associations were not evident in adjusted analyses ($P = .11$ and $P = .71$, respectively). With the exception of pretreatment HIV-1 RNA level, there was no evidence to suggest changing covariate effect of time (ie, violation of the proportional hazards assumption) for any of the final model covariates (HIV-1 RNA level, $P = .08$; race, $P = .87$; other covariates $P > .10$). Whereas a higher pretreatment HIV-1 RNA level was associated with an increased

hazard of virologic failure over the first 6 months of treatment, this effect weakened over time (Figure 3*B*). There was no evidence of modification of the race effect by any of the final model covariates (all tests for interaction, $P > .10$). Consistent results were observed for analyses of secondary as-treated virologic failure and regimen completion endpoints (Supplementary Figure 1, adjusted analyses not shown) and for sensitivity analyses.

Although no differences by race in CD4 cell count change were detected to weeks 24 or 48, black race was associated with a modestly greater increase from baseline to 96 weeks and beyond ($P < .001$; Figure 4). In adjusted analyses based on CD4 cell count change from baseline to week 96, blacks had a 33 cells/µL (95% CI, 16–50 cells/µL) larger increase compared to whites. Factors associated with smaller CD4 cell count increases over 96 weeks included male sex ($P < .001$), older age ($P = .03$), and hepatitis C antibody ($P = .004$); lower pretreatment HIV-1 RNA level was associated with larger CD4 cell count changes over 96 weeks ($P < .001$). Given the differences in the racial subgroups with respect to pretreatment CD4 cell count and sex, interactions of these variables and race were evaluated, but not found ($P = .10$ and $P = .65$, respectively). Similar results were obtained in failure-time analyses of time to CD4 count increase >250 cells/µL, although the effect of race in these analyses was not significant (HR, 1.1 [95% CI, .97–1.2], $P = .14$).

DISCUSSION

Our analysis of 2495 HIV-infected ART-naive individuals randomized to 15 different initial ART treatment regimens on 5 ACTG clinical trials and followed for a median of almost 3 years demonstrates a 40% greater hazard of virologic failure for blacks compared to whites. Other factors associated with an
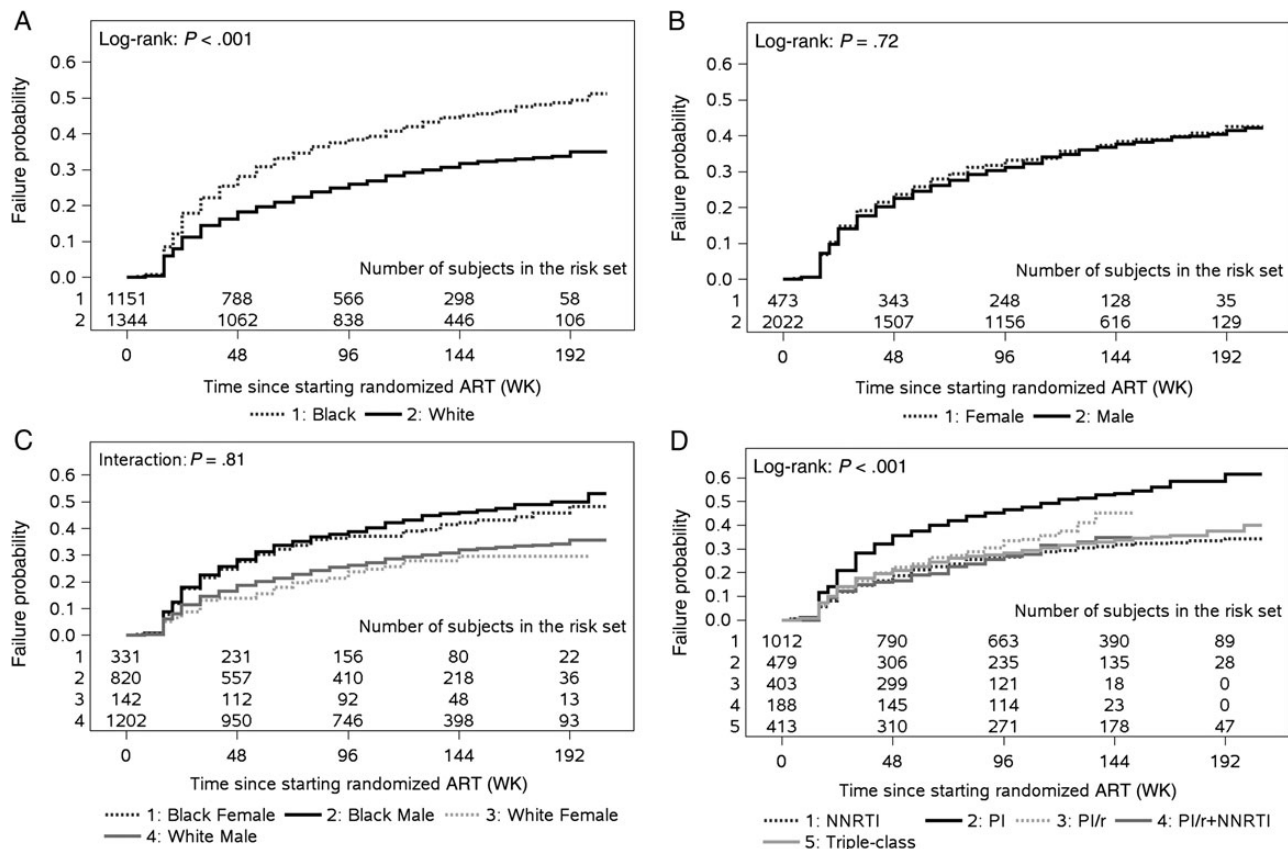
Figure 2. Failure-time distributions. Cumulative probability of time to virologic failure (intention-to-treat) by race (*A*), sex (*B*), race and sex (*C*), and class of randomized antiretroviral treatment (*D*). Abbreviations: ART, antiretroviral therapy; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PI/r, PI taken with low-dose ritonavir for pharmacological boosting.

increased hazard of virologic failure included younger age, higher pretreatment HIV-1 RNA level, lower pretreatment CD4 cell count, hepatitis C antibody, less education, and recent nonadherence. Notably, most of these factors were more prevalent among blacks (except age and HIV-1 RNA), but the association of black race with increased virologic failure persisted in adjusted analyses. Similar results were seen in sensitivity analyses using alternate endpoints of as-treated virologic failure and regimen completion.

The effect of race was observed consistently across a range of ART regimens despite differences in virologic failure rates across the regimens. These included regimens that were NNRTI-, PI-, and PI/r-based, as well as NRTI-sparing and triple-class (NRTI, NNRTI, and PI) regimens. Given the different mechanisms of action and pharmacokinetic properties of the drugs, this finding adds strength to the hypothesis that racial differences are driven by unmeasured social factors, rather than solely by differences in biological factors, such as metabolism and tolerability.

Access to care may contribute to racial disparities in ART outcomes [9–11, 27]. Although our clinical trials setting provided free and ready access to ART with support from the site staff, it is likely that disparities in other external factors, such as availability of transportation to the clinic, inflexible work schedules, access to childcare facilities, and other social factors, still exist that have an impact on an individual's response to ART [28, 29]. We also assessed self-reported satisfaction with social support in a subset of participants and found that although a lower proportion of black women reported being at least "somewhat satisfied" with their support from family members and friends compared to white women, there was little difference by race among men. Lower satisfaction with support was associated with increased risk of virologic failure; however, this association was not significant in adjusted analyses.

Mistrust of medical establishment and research may disproportionately affect blacks compared to whites [30, 31]. In our cohort, a greater proportion of black men reported being "not at all" or only "somewhat" sure that the study medication they were receiving would have a positive effect on their health compared with white men and all women. Although not significant in multivariable analysis, in unadjusted analysis a lower
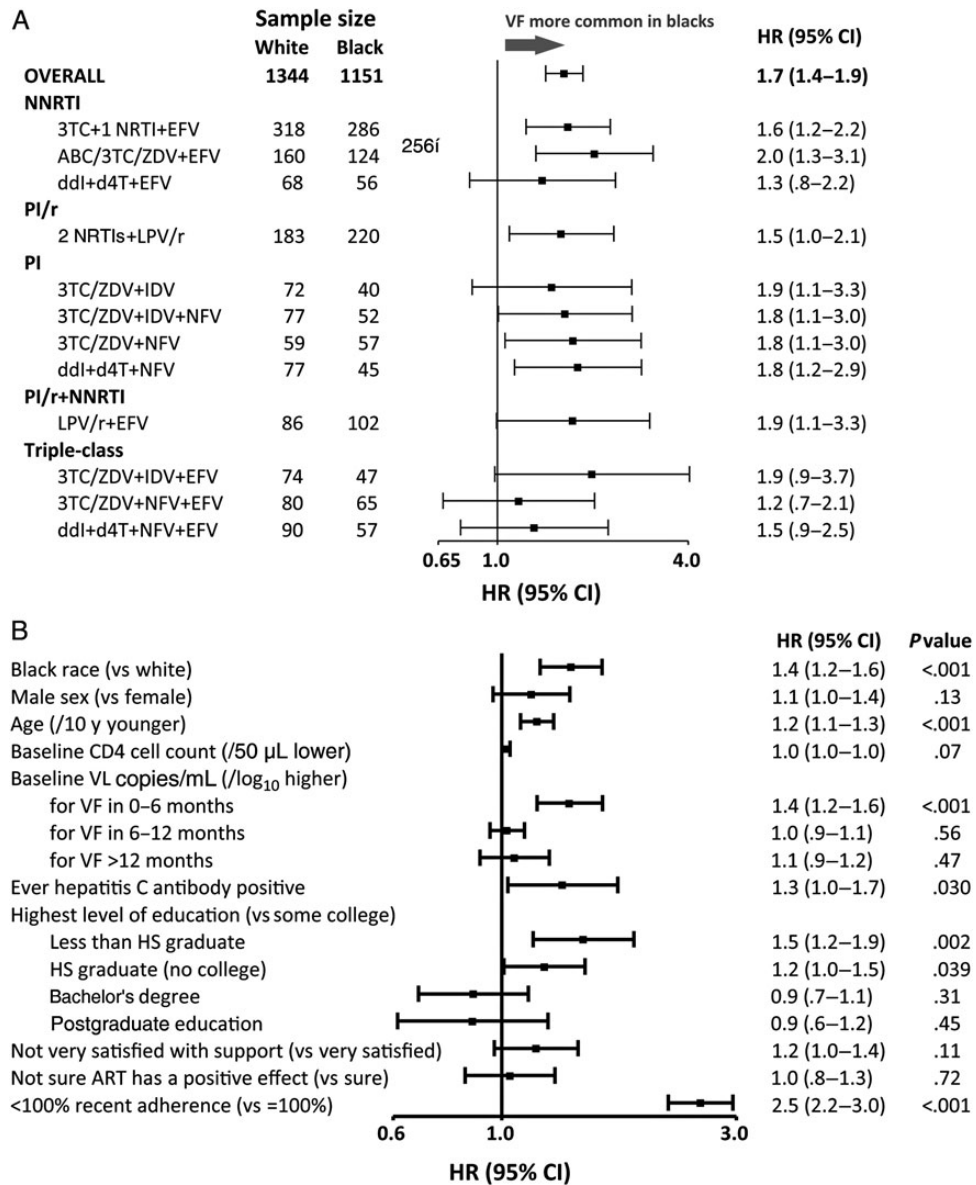
Figure 3. Relative hazard (unadjusted) of virologic failure. Forest plot showing the estimated hazard ratio and 95% confidence interval of virologic failure (intention-to-treat). *A*, Unadjusted with estimates given overall (stratified by randomized antiretroviral therapy [ART]) and by randomized ART (N = 2495). *B*, Adjusted for covariates shown (n = 2492). Recent adherence is based on the most recent self-report adherence assessment over a 4-day recall period. Provider choice of nucleoside reverse transcriptase inhibitor (A5073), stavudine extended release (XR) or tenofovir or (A5142) zidovudine, stavudine XR, or tenofovir made prior to randomization. Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; CI, confidence interval; d4T, stavudine; ddI, didanosine; EFV, efavirenz; HR, hazard ratio; HS, high school; IDV, indinavir; LPV, lopinavir; LPV/r, lopinavir-ritonavir; NFV, nelfinavir; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PI/r, PI taken with low-dose ritonavir for pharmacological boosting; VF, virologic failure; ZDV, zidovudine.

perception that ART would positively benefit health was associated with increased risk of virologic failure.

In contrast to the observed higher risk of virologic failure, black race also was associated with a greater increase in CD4 cell count over 2 years. This finding is not completely understood, but the effect was modest and of questionable clinical

significance. No difference by race was observed in the time to CD4 count increase >250 cells/μL.

Not unexpectedly, lower 4-day self-reported medication adherence was the strongest predictor of virologic failure. The association of adherence and race is controversial. Although some studies have linked race to adherence, others found no
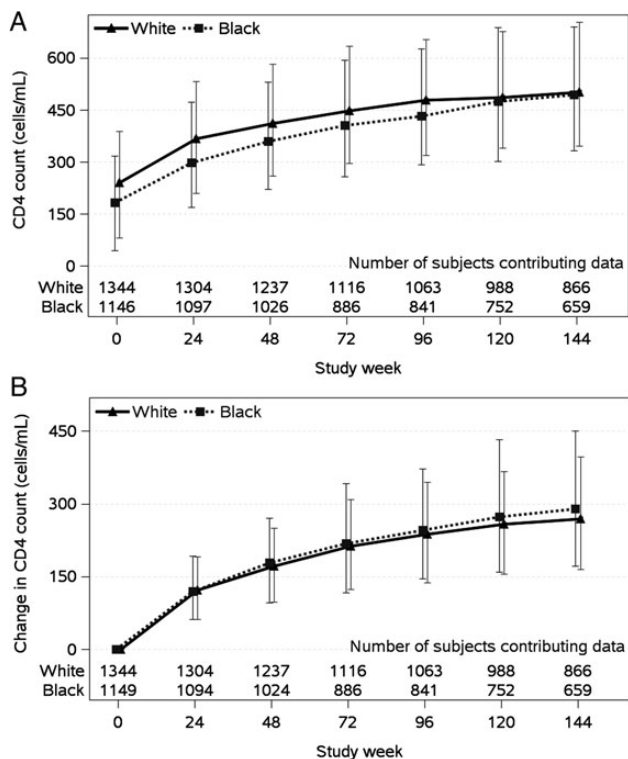
Figure 4. CD4 cell count changes over time.

association after controlling for confounders such as substance use, low health literacy, and depression [6, 32–36]. Although self-reported rates of medication adherence were high in our cohort, in unadjusted analyses lower adherence was reported by blacks than by whites. Importantly, after adjusting for recent adherence, the disparity by race persisted.

Some associations between black race and virologic failure that were reported in individual trials were not observed in this study. An interaction between race and adherence that suggested a greater effect of nonadherence on virologic failure in blacks than whites was reported in a secondary analyses of one of the studies included in the present analysis (A5095) [14], but not in the current study. Because A5095 was a study of efavirenz-based ART, one hypothesis for the interaction was that it was attributable to a genetic polymorphism that is more common in blacks and results in higher efavirenz concentrations [37] that may increase side effects and medication discontinuation. Although this effect could be masked in our analysis that included non-efavirenz-containing regimens, in an exploratory post hoc analysis, a 3-way interaction between race, adherence, and an indicator for efavirenz-containing regimen was not found (P = .75). In a prior analysis of study ACTG 384, greater racial disparity was associated with lower education [13]. Compared to white men, a lower proportion of all blacks

and white women reported education beyond high school in the present study, and although lower education was associated with an increasing risk of virologic failure, an interaction between race and education level was not detected.

Strengths of this study include the average length of follow-up of nearly 3 years; the inclusion of important demographic, clinical, and socioeconomic factors as well as assessments of self-efficacy and adherence; and the structured clinical trial setting that provided comparable data collection across all studies. This study had a large sample size, with significant representation from blacks at 55 sites across the United States, where HIV infection is predominantly with clade B virus [38]. Although 2 international sites, Italy (n = 127, 98% white) and Johannesburg (n = 36, 100% black), were included, the results were unchanged in sensitivity analyses excluding these individuals. Our findings are strengthened by the consistency of results across 3 distinct virologic failure endpoints (intention-to-treat, as-treated, and regimen completion).

One limitation of our study is that our study population may not be representative of the population at large. Clinical trials often attract an adherent, committed, and generally healthier population, and participation in a trial implies a degree of trust in the healthcare system. Racial differences persisted despite this. Other limitations include the exclusion of Hispanics; the inclusion of older regimens that are no longer used (eg, unboosted PIs and triple-class regimens); limited information on socioeconomic factors that could be residual confounders such as income, housing, and life issues; and that documentation of pretreatment confounders by self-report was available for only approximately half of subjects and limited primarily to studies conducted in the late 1990s. Sensitivity analyses restricted to individuals with full data available for the socioeconomic factors of interest and excluding those randomized to unboosted PI regimens yielded conclusions consistent with our main findings.

In summary, in this analysis of randomized ACTG studies, black race was associated with a 40% higher risk of virologic failure on initial ART regimens compared to white race. This finding was not fully explained by demographic, clinical, socioeconomic, and adherence factors that were captured in the study and found to be associated with both race and virologic failure. The consistency of the observation over a range of regimens suggests that it may be driven by unmeasured social factors, although biological factors cannot be ruled out. Future studies should investigate issues contributing to racial disparities in ART outcomes so that effective intervention strategies can be developed to close this gap.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted

materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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