

Race and Sex Differences in Antiretroviral Therapy Use and Mortality among HIV-Infected Persons in Care

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Background. There are conflicting data regarding race, sex, and mortality among persons infected with human immunodeficiency virus (HIV). We studied all-cause mortality among persons in care during the highly-active antiretroviral therapy (HAART) era.

Methods. This retrospective cohort study included patients who made ≥ 1 clinic visit from January 1998 through December 2005.

Results. Of 2605 patients (with 6657 person-years of follow-up), 38% were black and 24% were female. The percentage of time in care while receiving HAART was lower for blacks than for nonblacks (47% vs. 76%; $P < .001$) and for females than for males (57% vs. 71%; $P = .01$). There were 253 deaths (38 per 1000 person-years). After adjustment for characteristics at baseline, death was associated with black race (hazard ratio [HR], 1.33; $P = .04$), female sex (HR, 1.53; $P = .007$), injection drug use (IDU) as a risk factor for HIV infection (HR, 1.61; $P = .009$), older age (HR, 1.45 per 10 years; $P < .001$), a lower CD4 cell count (HR, 0.59 for 200 vs. 350 cells/mm³; $P < .001$) and a higher HIV type 1 RNA level (HR, 1.35; $P < .001$). After adjustment for the length of time that HAART was received, black race (HR, 1.00; $P = .99$) and IDU (HR, 1.37; $P = .09$) were no longer associated with death, but female sex was (HR, 1.62; $P = .002$).

Conclusions. Race-associated differences in mortality likely resulted from HAART use. Women had an increased risk of death even after adjustment for HAART use. Addressing racial disparities will require improved HAART utilization. Increased mortality among women requires further study.

Highly active antiretroviral therapy (HAART) has dramatically decreased morbidity and mortality among HIV-infected individuals living in many countries [1, 2]. Effective antiretroviral therapy (ART) clearly delays the progression of HIV-related disease and prolongs survival [2], but these survival benefits have not been equitably distributed by race and sex [3, 4].

Among all persons in the United States with AIDS, blacks consistently have a poorer long-term survival than do nonblacks [5]. Both before and after the introduction of HAART, population-based studies in the United States found significant race and sex differences in HIV-associated mortality [4, 6]. These survival differences, however, may be attributed to disparities in access to medical care and utilization of HAART; it remains unclear whether race and sex differences in survival exist for patients once they are established in care. In the pre-HAART era, a study of HIV disease progression and survival of patients at a single urban center found no significant demographic differences in mortality [7]. After the introduction of HAART, however, national disparities in mortality between black and white persons widened significantly, especially among women and elderly individuals [3]. Several studies found that HIV-infected women and blacks are less likely to receive HAART than are HIV-infected men

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and whites, respectively, even among patients in care [8–13]. The effect of these differences on mortality has been inconclusive, however. In a Canadian study, in which there was free access to antiretroviral agents, women were significantly less likely to start receiving HAART, but there was no sex difference with regard to disease progression [10]. A study from an urban clinic investigating progression of HIV disease in the HAART era found that, compared with men, women had lower rates of HAART utilization and disease-free survival, but no significant race differences in survival were detected; receipt of HAART by race was not reported [14].

We therefore assessed all-cause mortality among HIV-infected persons enrolled in care during the HAART era. We compared HAART utilization and mortality rates by race and sex, and we examined the demographic and clinical characteristics associated with time to death.

MATERIALS AND METHODS

Study population. We conducted a retrospective observational cohort study among persons in care at the Comprehensive Care Center (CCC), a Vanderbilt University–affiliated outpatient clinic in Nashville, Tennessee, which provides primary and subspecialty care for HIV-infected persons. The study population included all patients who established care and made at least 1 provider visit between 1 January 1998 and 31 December 2005. Follow-up ended at death, on 31 December 2005, or at

the last clinic visit (for persons with no clinic visit for >1 year by 31 December 2005). During the study period, health care coverage was available to virtually all HIV-infected Tennesseans [15].

Data collection. The main outcome measurement was all-cause mortality. Information on death was obtained from an electronic database and review of medical records. The database was routinely updated based on reports from families, local newspapers, hospitals, and the Social Security Death Index. Deceased patients were included in the study only if they were seen at the Comprehensive Care Center within 1 year of their death. Persons who died ≥ 12 months after their last clinic visit were considered to be lost to follow-up and were treated in the same manner as other individuals not seen for ≥ 12 months (i.e., those for whom follow-up ended at the last clinic visit). A validated form ascertaining cause of death was used to identify causes of death [16]. The immediate cause of death, if available, was classified as AIDS related or non-AIDS related, on the basis of the US Centers for Disease Control and Prevention (CDC) list of AIDS-defining conditions [17].

The following demographic and clinical characteristics were also assessed: age at enrollment (at the time of the first clinic visit), sex, race, self-reported probable route of HIV infection, CD4⁺ lymphocyte count and CD4⁺ lymphocyte percentage (CD4%) at enrollment, HIV-1 RNA level at enrollment, hepatitis C virus infection, and diagnosis of AIDS at or before

Table 1. Characteristics of the patients at baseline, by race and sex.

Characteristic	Black (n = 989)	Nonblack (n = 1616)	P	Female (n = 617)	Male (n = 1988)	P
Sex, female	316 (32.0)	301 (18.6)	<.001	NA	NA	
Black race	NA	NA	...	316 (51.2)	673 (33.9)	<.001
Age at first visit, median (IQR), years	37.9 (30.6–44.4)	37.4 (31.5–43.0)	.41	35.4 (28.4–42.6)	38.2 (32.1–43.4)	<.001
IDU as risk factor for HIV infection	139 (14.1)	169 (10.5)	.007	77 (12.5)	231 (11.6)	.57
Baseline value						
CD4 ⁺ lymphocyte						
Count, median (IQR), cells/mm ³	304 (134–494)	336 (154–533)	.003	366 (192–576)	312 (135–506)	<.001
Percentage, median (IQR)	20 (11–29)	22 (13–31)	.005	24 (15–33)	20 (11–29)	<.001
HIV-1 RNA level, median (IQR), log ₁₀ copies/mL	4.4 (3.4–5.0)	4.3 (2.9–4.9)	.002	4.1 (2.9–4.8)	4.4 (3.2–5.0)	<.001
AIDS diagnosis before first visit, %	88 (8.9)	180 (11.1)	.07	39 (6.3)	229 (11.5)	<.001
ART/HAART exposure before first visit	282 (28.5)	692 (42.8)	<.001	208 (33.7)	766 (38.5)	.03
HCV infection	124 (12.5)	106 (6.6)	<.001	78 (12.6)	152 (7.6)	<.001
History of substance abuse ^a						
IDU	127 (17.4)	150 (12.8)	.002	64 (14.2)	213 (14.7)	.004
Non-IDU	336 (46.0)	512 (43.7)		173 (38.4)	675 (46.5)	
None	237 (36.6)	509 (43.5)		213 (47.3)	563 (38.8)	
Data missing	289	445		167	537	

Note. Data are the no. (%) of patients, unless otherwise indicated. ART, antiretroviral therapy; HAART, highly active antiretroviral therapy; HCV, hepatitis C virus; IDU, injection drug use; IQR, interquartile range; NA, not available.

^a For this characteristic, the percentages are of only those patients for whom data were available: n = 700 and 1171 for black and nonblack, respectively; and n = 450 and 1451 for female and male, respectively.

Table 2. Characteristics of patients while they were receiving care, including utilization of highly active antiretroviral therapy (HAART), by race and sex

Characteristic	Black (n = 989)	Nonblack (n = 1616)	P	Female (n = 617)	Male (n = 1988)	P
Follow-up time, years	2.11 (0.54–4.32)	1.96 (0.63–4.06)	.75	2.14 (0.57–4.34)	2.00 (0.60–4.08)	.28
Time to HAART initiation, ^a days	21 (0–113)	9 (0–51)	<.001	16 (0–82)	14 (0–67)	.14
Percentage of time in care while receiving HAART	47 (0–94.5)	76 (0–98.9)	<.001	57 (0–95.9)	71 (0–98.2)	.012

Note. Data are median values (interquartile range [IQR]). HAART, highly active antiretroviral therapy; visit, clinic visit.

^a Among patients who received HAART (n = 1821).

enrollment (as determined by the CDC classification criteria [17], excluding a CD4⁺ lymphocyte count of <200 cells/mm³). In addition, variables related to HAART utilization were obtained, including: HAART or ART (i.e., non-HAART antiretroviral therapy) exposure before enrollment, HAART use while receiving care, and the percentage of time receiving HAART while in care. The latter variable was defined as the total number of days receiving HAART divided by the total number of days in care (from the time of the first clinic visit to the end of follow-up, as defined above). HAART was defined as regimens of 7 days' duration that contained 2 nucleoside reverse-transcriptase inhibitors (NRTIs) plus either a protease inhibitor (PI), a nonnucleoside reverse-transcriptase inhibitor (NNRTI), or a third NRTI; 1 NRTI, 1 PI, and 1 NNRTI; 2 PIs plus 1 NRTI or NNRTI; or any regimen containing enfuvirtide. Non-HAART ART included mono- or dual-NRTI therapy. History

of injection drug and non-injection drug abuse was also collected for a subset of patients who had ≥2 provider clinic visits between 1 January 1999 and 31 December 2004.

Medical providers entered clinical data into an electronic medical record at the time of the patient encounter; automated data upload was used to enter laboratory results, and clinic personnel entered data on deaths. Laboratory data and all information on ART use (including treatment start and stop dates) were validated by systematic chart review. If the chart noted (by patient self-report and/or by provider observation) that the patient had not been taking the prescribed antiretroviral therapy, the patient was coded as not taking ART during that period. All treatment decisions regarding ART were made in a case conference setting.

The study protocol was approved by the institutional review board of Vanderbilt University Medical Center. Clinical research

Table 3. Cox proportional hazards model of factors associated with initiation of highly active antiretroviral therapy (HAART).

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Black race	0.76 (0.69–0.83)	<.001	0.87 (0.79–0.97)	.009
Female sex	0.88 (0.79–0.97)	.027	1.06 (0.95–1.19)	.30
IDU as risk factor for HIV infection	0.93 (0.81–1.07)	.29	0.84 (0.72–0.98)	.030
AIDS diagnosis before first visit	2.02 (1.76–2.32)	<.001	1.24 (1.07–1.45)	.005
Age at first visit ^a	1.18 (1.13–1.24)	<.001	1.06 (1.01–1.11)	.027
Baseline value				
CD4 ⁺ lymphocyte				
Count		<.001		<.001
200 vs. 350 cells/mm ³	0.74 (0.71–0.77)		0.86 (0.79–0.93)	
200 vs. 500 cells/mm ³	0.61 (0.57–0.65)		0.75 (0.66–0.85)	
Percentage ^b	0.71 (0.68–0.74)	<.001	0.84 (0.78–0.92)	<.001
HIV-1 RNA level		<.001		<.001
3 vs. 4 log ₁₀ copies/mL	0.54 (0.51–0.57)		0.60 (0.57–0.64)	
5 vs. 4 log ₁₀ copies/mL	0.77 (0.72–0.81)		0.91 (0.85–0.98)	
ART/HAART exposure before first visit	3.5 (3.19–3.85)	<.001	2.64 (2.37–2.93)	<.001
HCV infection	0.62 (0.53–0.74)	<.001	0.83 (0.69–1.00)	.051

Note. ART, antiretroviral therapy; CI, confidence interval; HAART, highly active antiretroviral therapy; HCV, hepatitis C virus; HR, hazard ratio; visit, clinic visit.

^a Per 10 years.

^b Per 10 units.

Table 4. Deaths, by race and sex of patients.

Deaths	All races (<i>n</i> = 253)	Black (<i>n</i> = 127)	Nonblack (<i>n</i> = 126)	<i>P</i>	Female (<i>n</i> = 67)	Male (<i>n</i> = 186)	<i>P</i>
Per 1000 person-years	38	49	31	<.001	41	37	.47
For which info. on cause was available	211 (83.4)	108 (85.0)	103 (81.7)		56 (83.4)	155 (83.3)	
AIDS related	114 (54.0)	52 (48.1)	62 (60.2)	.11	33 (58.9)	81 (52.3)	.48

Note. Data are the no. (%) of subjects who died, unless otherwise indicated.

was conducted in accordance with the human experimentation guidelines of the US Department of Health and Human Services and Vanderbilt University.

Statistical analysis. Fisher's exact test compared categorical variables, and the Mann-Whitney *U* test compared continuous variables, including characteristics at baseline and utilization of HAART during follow-up. Cox proportional hazards models were constructed to examine factors associated with time to HAART initiation and with time to death. The model of factors associated with time to HAART initiation and the first model of factors associated with time to death included only the variables for which information was available at baseline (i.e., age, race, sex, injection drug use [IDU] as a risk factor for HIV infection, previous diagnosis of AIDS, hepatitis C virus infection, CD4⁺ lymphocyte count, CD4%, HIV-1 RNA level, and previous HAART/ART use); the second model of time to death also included the percentage of time receiving HAART after the first clinic visit. All variables were included in the multivariate model, regardless of their statistical significance in the univariate analysis. Continuous predictors were not categorized. The CD4⁺ lymphocyte count (in all models) and the HIV-1 RNA level (in the time-to-HAART-initiation model) were expanded using restricted cubic splines with 3 knots to account for nonlinearity. There was little evidence of nonlinearity in the association between death and HIV-1 RNA level, CD4%, age, and percentage of time receiving HAART (*P* > .5, for each), so the association between the hazard of death and these variables was assumed to be linear. There were no significant interactions between sex and race in either model. The analysis was performed using Stata software (version 9.0; Stata) and R software (version 2.6.2) [18].

RESULTS

There were 2605 patients who met the criteria for inclusion in the study. The demographic characteristics of the study population are shown in table 1. Among the entire population, the median age was 38 years; 38% of the population was black, 24% was female, and 12% reported IDU as their risk factor for HIV transmission. Blacks presented with a lower median CD4⁺ lymphocyte count and CD4% and a higher median HIV-1 RNA level than did nonblacks. Blacks were also less likely to have been exposed to ART or HAART before their first clinic

visit, and they were more likely to have reported IDU as their risk factor for HIV transmission. Women (compared with men) presented at a younger median age than men and had a higher median CD4⁺ T lymphocyte count and CD4%, as well as a lower median baseline HIV-1 RNA level. Women were less likely to have had AIDS diagnosed at or before the first CCC visit, and they were less likely to have had previous exposure to ART or HAART.

The median follow-up was 2.03 years (interquartile range [IQR], 0.60–4.17 years) after the first clinic visit; there were 6657 person-years of follow-up. Thirty percent (*n* = 773) of patients were lost to follow-up. Loss to follow-up did not differ by race or sex. Among the 1821 patients who started (or continued) receiving HAART during the study period, the time to initiation of HAART from the time of the first clinic visit was significantly longer for blacks than for nonblacks but was similar for females, compared with males (table 2). The percentage of time receiving HAART while in care was also less for blacks than for nonblacks, and it was also less for women than for men (table 2). The percentage of time receiving HAART while in care was also examined only for those individuals with a CD4⁺ lymphocyte count at baseline of <200 cells/mm³. Of 901

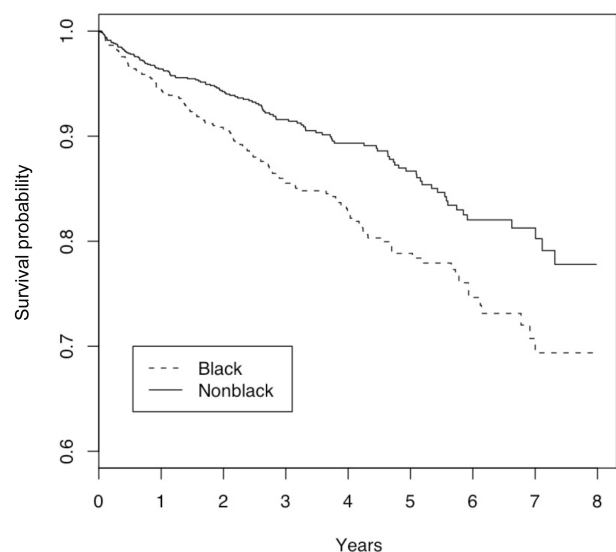


Figure 1. Kaplan-Meier survival curve of the time to death in the total cohort, by race.

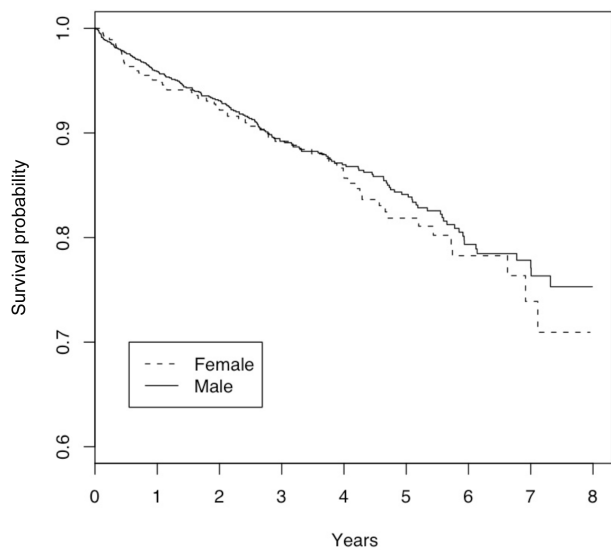


Figure 2. Kaplan-Meier survival curve of time to death in the total cohort, by sex.

such individuals, 358 (40%) were black and 185 (21%) were female. Within this group, the median percentage of time receiving HAART while in care was less for blacks than for non-blacks (75% vs. 91%; $P < .001$), and it was also less for females than for males (74% vs. 88%; $P = .009$).

In a multivariable Cox proportional hazards model that included all patients, initiation of HAART was associated with nonblack race, no history of IDU as a risk factor for HIV transmission, previous diagnosis of AIDS, older age at baseline, lower CD4⁺ lymphocyte count at baseline, lower CD4%, HIV-1 RNA level, and previous ART use (table 3). Sex was not associated with the time to initiation of HAART. A secondary multivariable analysis also adjusted for history of substance abuse (IDU, non-IDU substance abuse, or no substance abuse; IDU as a risk factor for HIV transmission was not included in this secondary model) for those patients for whom this information was available (i.e., 1901 patients [73% of subjects]). Not starting HAART was associated with a history of IDU ($P < .001$) and was weakly associated with a history of non-IDU substance abuse ($P = .058$). Race was no longer significantly associated with time to initiation of HAART ($P = .14$), although, for blacks, the hazard ratio (HR) for initiating HAART was approximately the same as that presented in table 3 (HR, 0.91; 95% CI, 0.81–1.03).

A total of 253 deaths occurred (mortality rate, 38 deaths/1000 person-years) (table 4). The crude all-cause mortality rate was higher for blacks than for nonblacks (HR, 1.6; $P < .001$) but was similar for females and males (HR, 1.1; $P = .47$). Kaplan-Meier survival curves, by race and by sex, are shown in figures 1 and 2, respectively.

Information on cause of death was available for 83% of the

deceased patients (table 4). Of the individuals for whom information on the cause of death was available, 54% died of an AIDS-related cause. The proportion of AIDS-related deaths was not statistically different between blacks and nonblacks ($P = .11$) or between females and males ($P = .48$) (table 4).

In a multivariable Cox proportional hazards model that adjusted for characteristics noted at the first clinic visit, death was associated with older age, black race, female sex, IDU as a risk factor for HIV transmission, a lower CD4⁺ T lymphocyte count at baseline, and a higher HIV-1 RNA level (table 5). All associations were similar after adjusting for a history of IDU or non-IDU substance abuse. In a second Cox proportional hazards model that also included the percentage of time receiving HAART, black race and IDU (as risk factors for HIV transmission) were no longer associated with death. Less time receiving HAART was associated with death as well as with older age, female sex, previous diagnosis of AIDS, and a lower CD4⁺ T lymphocyte count at baseline (table 5). Results were similar when a history of substance abuse was included. If those who were lost to follow-up actually died, then black race would still be associated with a higher mortality rate ($P = .038$), whereas female sex would not be ($P = .16$) (data not shown).

DISCUSSION

Among HIV-infected persons in care between 1998 and 2005, we found significant disparities in HAART utilization and survival according to race and sex. We found that women and blacks were less likely to receive HAART than were men and nonblacks, respectively. These associations persisted when they were limited to persons with a CD4⁺ lymphocyte count of <200 cells/mm³ at baseline. The crude all-cause mortality rate was higher in blacks than in nonblacks, and, when the data were adjusted for characteristics at noted at the first clinic visit (including the CD4⁺ lymphocyte count at baseline), death was associated with black race and female sex. When we adjusted for utilization of HAART while in care, black race was no longer associated, but female sex remained associated, with an increased risk of death. This finding suggests that differences in the use of HAART were at least partly responsible for the differences in mortality by race. The association between female sex and death, however, cannot be explained by differences in HAART use.

Although black patients initially presented with HIV disease that was at stages more advanced than those noted in nonblack patients, we found that black patients were slower to initiate HAART and were less likely to be receiving HAART while in care. Other studies conducted in the United States [19, 20] and the United Kingdom [21–23] have made similar observations in blacks presenting for care in more advanced stages of disease. In addition, many studies have shown a decreased use of

Table 5. Cox proportional hazards model of factors associated with death, at enrollment and when highly active antiretroviral therapy (HAART) is included.

Factor	Univariate analysis		Multivariate analysis	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
At enrollment				
Black race	1.61 (1.26–2.06)	<.001	1.33 (1.01–1.74)	.04
Female sex	1.11 (0.84–1.47)	.47	1.53 (1.13–2.08)	.007
IDU as a risk factor for HIV infection	1.73 (1.27–2.36)	<.001	1.61 (1.12–2.31)	.009
AIDS diagnosis before first visit	2.57 (1.92–3.43)	<.001	1.31 (0.94–1.82)	.11
Age at first visit ^a	1.44 (1.27–1.63)	<.001	1.45 (1.26–1.67)	<.001
Baseline value				
CD4 ⁺ lymphocyte count		<.001		<.001
200 vs. 350 cells/mm ³	0.56 (0.50–0.63)		0.59 (0.47–0.73)	
200 vs. 500 cells/mm ³	0.42 (0.35–0.50)		0.45 (0.31–0.64)	
CD4 ⁺ lymphocyte percentage ^b	0.58 (0.52–0.66)	<.001	1.10 (0.87–1.39)	.41
HIV-1 RNA level, log ₁₀ copies/mL	1.63 (1.42–1.88)	<.001	1.35 (1.15–1.57)	<.001
ART/HAART exposure before first visit	0.88 (0.68–1.14)	.32	1.29 (0.95–1.74)	.10
HCV infection	1.22 (0.85–1.76)	.28	1.05 (0.69–1.59)	.83
Including HAART				
Percentage of time in care while receiving HAART ^{c,d}	0.80 (0.77–0.83)	<.001
Black race	1.00 (0.76–1.32)	.99
Female sex	1.62 (1.19–2.21)	.002
IDU as risk factor for HIV infection	1.37 (0.95–1.97)	.09
AIDS diagnosis before first visit	1.53 (1.10–2.13)	.01
Age at first visit ^a	1.59 (1.38–1.83)	<.001
Baseline value				
CD4 ⁺ lymphocyte count		<.001
200 vs. 350 cells/mm ³	0.50 (0.39–0.64)	
200 vs. 500 cells/mm ³	0.34 (0.23–0.49)	
CD4 ⁺ lymphocyte percentage ^b	0.97 (0.75–1.25)	.83
HIV-1 RNA level, log ₁₀ copies/mL	1.29 (1.10–1.51)	.002
ART/HAART exposure before first visit	1.44 (1.07–1.95)	.02
HCV infection	0.86 (0.59–1.31)	.47

Note. ART, antiretroviral therapy; CI, confidence interval; HCV, hepatitis C virus; HR, hazard ratio; IDU, injection drug use; visit, clinic visit.

^a Per 10 years.

^b Per 10 units.

^c Per 10% increase.

^d Univariate HR per 10% increase: 0.91 (95% CI, 0.88–0.94) (*P* < .001).

HAART among blacks and other ethnic minorities [11, 12, 24] and increased rates of discontinuation [25–27].

In our cohort, women presented at earlier stages of HIV disease than did men. This result is consistent with findings reported from another study in the southeastern United States [28]. Like blacks, however, women were also less likely to use HAART—even among only those patients with a CD4⁺ lymphocyte count of <200 cells/mm³ at baseline. Other studies have shown sex differences in HAART prescription and utilization [8, 9, 11, 29, 30], even among patients with free access to antiretroviral agents [10].

The reasons for disparity in HAART utilization in this cohort of patients are unclear. During the study period, all patients had health care coverage that included HIV-related care. All

treatment decisions regarding ART were made in a case conference setting. Patients were brought to conference by providers when their immunologic, virologic, or clinical status warranted discussion of starting or changing antiretroviral therapy. The most common reasons for delay of referral to a case conference included lack of regular follow-up, active substance abuse, or a patient's wish to not use ART. In the subset of patients for whom data were available, more blacks than non-blacks had a history of substance abuse, and, in our secondary analyses, which adjusted for history of substance abuse, race was no longer statistically significant (*P* = .14). However, because the hazard ratios were quite similar (0.91 and 0.87, respectively, in the multivariable analyses adjusted and not adjusted for history of substance abuse), the lack of statistical

significance may be caused, in part, by the decreased power. Data regarding the history of substance abuse were missing for 27% of our patients.

Regardless of the reasons that patients did not start receiving HAART, the present study suggests that increased utilization of HAART by black patients could improve disparities in disease progression. We found that black race was associated with increased mortality, although not after adjusting for HAART use. Other large, population-based studies have shown increased HIV-associated mortality among blacks [5, 6, 31, 32]. It has been reasoned that survival differences in these population-based studies can be attributed to disparities in *access* to care and that they might not be present among patients *in care* [7, 14, 33–35]. In contrast, our findings suggest that racial differences in treatment while in care also influence survival.

In the present study, we also found that female sex was associated with increased mortality, but this association remained even after adjustment for HAART use. Studies from the early 1990s found that women with AIDS had a shorter survival time than did men [36–38]; however, as with blacks, this was attributed to inequalities in access to health care [39]. Many studies, both before and after the HAART era, have not found any sex differences in HIV-associated mortality [7, 40–42]. A few studies from the HAART era, however, have found similar sex differences in survival and disease progression among patients in care [14, 43]. Female sex was associated with lower rates of treatment, increased disease progression, and decreased survival in the HAART era (1996–1999) at the Johns Hopkins HIV clinic, but not in the pre-HAART era (1990–1995) [14]. After adjustment for receipt of HAART and for achieving an undetectable HIV-1 RNA level, the differences by sex were no longer as significant. A recent study from Sao Paulo, Brazil, found that, even though women were admitted to the clinic while in the earlier stages of HIV disease, female sex was associated with AIDS-related death after adjustment for prescribed antiretroviral therapy (HR, 1.86); there was no significant sex difference in the use of ART, after patients were stratified according to their clinical status [43].

Other reasons, in addition to decreased HAART utilization, must be explored to explain this increase in mortality among women. Possible factors might include adherence and response to HAART, as well as psychosocial factors, such as active substance abuse, lack of social support, and depression. A study comparing mortality rates in the Multicenter AIDS Cohort Study (men) and the Women's Interagency HIV Study found that rates of accident- or injury-related death were higher among women. In addition, risk factors for death among women included unemployment, higher level of alcohol use, and IDU [44].

Of the deceased individuals in our cohort for whom information on cause of death was available, 54% died of an AIDS-

related cause. This finding is consistent with other studies of cause of death conducted in the HAART era, in which 38%–71% of the deaths were AIDS related [45–48]. In the present study, the proportion of AIDS-related deaths did not differ by race or sex.

There are several limitations of the study. Our data were retrospective from a single outpatient clinic and thus cannot necessarily be generalized to other US or international populations. Rates of loss to follow-up were high, but they did not differ by race or sex. We were unable to ascertain whether a lost patient transferred to another clinic. Although we included many clinical variables previously found to be associated with survival, there are many additional factors, which were not systematically recorded, that may affect the survival of HIV-infected individuals. We did not have information on why persons were not receiving HAART (i.e., patient vs. provider preference). Although insurance status was not specifically evaluated, health care coverage was available to virtually all HIV-positive Tennesseans during the study [15], and formulary availability, laboratory testing, appointment scheduling, and treatment protocols were equivalent for all patients.

In conclusion, the present study provides evidence that significant disparities in HAART utilization and survival by race and sex do exist among HIV-infected persons receiving care. The reasons for sex differences in survival remain unclear. Further studies are warranted to identify additional factors that are associated with increased mortality among women.

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