Paying the Price for Late Starts and Early Stops: Racial and Sex Disparities in HIV-Related Mortality

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(See the article by Losina et al, on pages 1570–8.)

It is well documented that black and Hispanic individuals are significantly over-represented among individuals with human immunodeficiency virus (HIV) infection and/or AIDS in the United States. Equally concerning is the fact that black individuals who are infected with HIV, compared with their white counterparts, have a higher mortality rate and shorter time to death after HIV diagnosis. After the introduction of highly active antiretroviral therapy (HAART) in 1996, AIDS-related mortality decreased significantly until 1998, at which point it leveled off, remaining essentially unchanged through 2005. The percentage of decrease was smallest for black individuals, particularly black women, who experienced a 44% decrease, compared with a 79% decrease among white men [1]. In 2007, 9436 black or Hispanic individuals died as a result of HIV-related disease; this is more than double the number of white individuals who died of such causes in the same year [2]. Eighty-four percent of white patients survived >36 months after receiving a diagnosis of HIV infection, compared with 85% of Hispanic patients and 79% of black patients. Notably, 13% of black patients, compared with 11% of white patients and 10% of Hispanic patients, died within 12 months after receiving a diagnosis of HIV infection [2].

The study by Losina et al [3] uses a state-transition model to estimate the expected life expectancy loss due to HIV disease, HIV-associated behavioral risk, late presentation to treatment, and early discontinuation of HIV care and to compare these survival losses by race and sex. The study estimates that HIV-associated survival loss is indeed increased in blacks and Hispanics and that the loss is greatest among women in these minority groups. This study adds substantially to the mounting body of literature that describes disparities in HIV-related outcomes by race and sex. Specifically, the study finds that, if all HIV-infected persons initiated therapy according to the treatment guidelines, HIV disease would lead to an estimated 11.92 life-years lost per person, and late initiation of ART would lead to additional loss of 3.3 life-years per person for black individuals, 3.55 life-years per person for Hispanic individuals, and 2.63 life-years per person for white individuals. Importantly, black and Hispanic individuals were significantly more likely than white individuals to initiate therapy very late, with CD4+ cell counts <50 cells/μL (22.3% and 20.7% of patients vs 13.6% of patients) [3]. Other studies have clearly described the high prevalence of late presentation among black and Hispanic patients. A study conducted by the Centers for Disease Control and Prevention (CDC) reported that 56% of “late testers” (ie, those who received a diagnosis of AIDS within 1 year after having received a diagnosis of HIV infection) were black [4]. McNaghten and colleagues [5] evaluated data from 4379 HIV-infected patients who participated in the Adult and Adolescent Spectrum of HIV Disease project from 1996 through 2000 to determine at which point in their illnesses they initiated antiretroviral therapy. They found that Hispanic and black patients were 1.74 and 1.65 times more likely, respectively, to initiate HAART late (with CD4+ cell counts <200 cells/μL), compared with white patients (P < .001). The Losina study [3] not only documents the higher prevalence of late initiation among black and Hispanic patients but also provides an important estimate of the consequences of late treatment that should further motivate us to be more aggressive in our case-finding efforts.

The authors suggest that improved implementation of the CDC guidelines for testing could lead to higher CD4+ cell counts at the time of diagnosis. Specifically, the CDC recommendation is that
screening for HIV infection should be performed routinely for all patients 13–64 years of age in an “opt-out” manner. That is, patients should be informed that HIV testing will be performed unless they refuse to undergo it [6]. This more aggressive testing strategy was an important move forward and may help to identify more HIV-infected individuals at earlier stages of disease and thus provide an opportunity for early treatment. Of course, broader testing does not address the other factors that may lead to late treatment in black and Hispanic individuals (eg, poorer access to care, lack of health insurance, language barriers, and lack of trust in the medical establishment). Nonetheless, identifying HIV-infected individuals sooner should allow more individuals to maximize the benefits from treatment. Losina et al [3] also suggest that adherence to the current treatment guidelines will result in greater reductions in survival loss. Although this is likely to be a correct assumption, this strategy may not go far enough. Recent data suggest that the risk of death is lowest among HIV-infected individuals who initiate therapy at CD4+ cell counts that are >500 cells/μL [7]. Although more studies that address the question of the optimal time to start antiretroviral therapy are underway, it is clear that the case for earlier treatment is getting stronger as regimen tolerability improves and the long-term consequences of delayed treatment of HIV disease are revealed. Thus, the combined strategies of aggressive case finding via op-out testing and earlier initiation of therapy could work together to decrease the gap in survival between HIV-infected and uninfected individuals.

The Losina model [3] also examines the impact of treatment discontinuation on survival. Premature discontinuation of therapy, defined as not continuing to the next regimen after experiencing failure of the current regimen, was associated with .91 and 1.05 additional life-years lost per person for black and Hispanic patients, respectively, compared with .82 life-years per person for white patients. Notably, treatment discontinuation rates and their consequences were highest for black and Hispanic women. This finding is consistent with data from the Women’s Interagency HIV Study (WIHS) which found that white women were statistically significantly less likely than black or Hispanic women to discontinue HAART (hazard ratio, 0.49; 95% confidence interval [CI], 0.32–0.75) and that those who discontinued HAART were at statistically significant higher risk of death (hazard ratio, 2.81; 95% CI, 1.82–4.34) [8]. Of course, this raises the question of what drives black and Hispanic women to discontinue therapy at higher rates than white women? Some studies have suggested that HIV-infected black and Hispanic women are disproportionately impacted by competing priorities that include child-care and providing food and shelter for themselves and their families, which may impede consistent adherence to ART [9]. Black and Hispanic women with HIV infection also have been shown to have a higher prevalence of depression, compared with their white counterparts [10]. Other factors, such as stable access to treatment, past or current use of illicit drugs, a history of physical or sexual abuse, and treatment intolerance may also play a role in excess treatment discontinuation among black and Hispanic women [11].

An additional important factor identified in the Losina model [3] is the loss of survival because of high-risk behavior, defined as being a man who has sex with men, injection drug use, having multiple sex partners, being a commercial sex worker, or having a history of sexually transmitted disease. A comparison of survival among the HIV-negative general population with that among HIV-negative persons with high-risk behaviors indicated a survival gap of 8.33 life-years per person. Although this finding is important, it is also important to note that, whether or not they engage in high-risk behaviors themselves, black and Hispanic patients are more likely than white patients to live in environments with elevated rates of crime, incarceration, poverty, and substance abuse, including alcoholism. These factors contribute to the gap in life expectancy that exists between black and Hispanic individuals and white individuals in the general population [12]. The addition of HIV infection to these risks adds synergistically to the survival gap. This is well illustrated in the study of causes of death during the HAART era among HIV-infected women in the WIHS cohort and HIV-infected men in the Multicenter AIDS Cohort Study (MACS) [13]. More than 80% of the HIV-infected women in the WIHS cohort are black or Hispanic. Sixty-three percent of the WIHS cohort had annual income <$10,000, and nearly 80% were unemployed. In comparison, ~22% of the patients who were included in the MACS cohort were black or Hispanic HIV-infected men. Only 8% of HIV-infected men in the MACS cohort had annual income <$10,000, and <14% were unemployed. Notably, rates of accidental or injury-related mortality were 2.96 deaths per 1000 person-years among HIV-infected women in the WIHS cohort, compared with 0.79 deaths per 1000 person-years among HIV-infected men in the MACS cohort. In a multivariable analysis, significant risk factors for death among the women in the WIHS cohort were decreased CD4+ T cell count, unemployment, higher alcohol use, and injection drug use. Strategies to eliminate the survival gap associated with high-risk behaviors and high-risk environments must go well beyond aggressive HIV case finding and earlier initiation of therapy. Policies that address unstable housing, incarceration, poverty, unemployment, and substance abuse in minority communities are desperately needed as a foundation on which improved HIV care can be provided and sustained.

Although the estimation of a greater survival loss among women and black and Hispanic individuals is concerning, it is possible that the model used in the study by Losina et al [3] may have underesti-
imated the sex and racial survival loss, because it uses data from the MACS cohort to estimate disease progression. The MACS cohort consists entirely of men and contains a disproportionate number of white individuals; thus, it may not be a completely accurate estimator of disease progression among women or minorities. A study by Anastos et al [14] that used data from the MACS and WIHS cohorts found that HIV RNA levels were 30%–50% higher in men than in women but that women experienced disease progression at lower viral loads. In addition, decreases in CD4+ cell counts were also more rapid in women. Further, the study by Losina et al [3] may underestimate the impact of racial differences in HIV-related comorbid conditions that disproportionately affect the black population, such as HIV-related nephropathy, HIV-related anemia, and hepatitis C virus coinfection.

Nonetheless, one cannot argue with the overall conclusion of the study [3], which is that there is a price to pay for late presentation to care and for treatment discontinuation and that burden weighs disproportionately on women and minorities. Our challenge as clinicians and researchers is to design and implement better strategies to identify HIV-infected individuals at earlier stages of disease and to provide the necessary support to enter and retain them in care. Improving the care for those with the most challenges raises the level of care for all, and that should be our goal.

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References


