

# Gender, Race, and Geography: Do They Matter in Primary Human Immunodeficiency Virus Infection?

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(See the article by Meditz et al, on pages 442–451.)

Gender and racial differences in CD4+ T cell counts and human immunodeficiency virus (HIV)-1 RNA levels among chronically HIV-infected persons have been shown to exist in multiple studies [1, 2], and although women have significantly lower plasma HIV-1 RNA levels than men, the rate of progression to AIDS is similar among men and women [1]. Similarly, several studies have suggested that blacks and Latinos have lower CD4+ T cell counts and higher viral loads at presentation, but this is likely due to delays in diagnosis and, thus, more advanced disease at presentation [2, 3]. The study by Meditz et al [4] in this issue of the *Journal* confirms and extends these findings by demonstrating that gender and racial differences are present in the earliest stages of infection—in those with acute and recent HIV infection [4]. Among untreated patients in their cohort, however, this difference disappeared after 24

weeks, and by week 104 of follow-up, women had higher viral loads than men. Their data also suggest that women report fewer symptoms associated with the acute retroviral syndrome, which may delay or complicate early diagnosis in this population. These biologic differences between races and genders remain unexplained; however, there is little indication that these findings have major clinical significance. Nevertheless, a better understanding of the biologic factors leading to these differences may give insight into HIV pathogenesis. Although the lessons to be learned may be important, the likelihood is low that these will lead to interventions that will change disease course in the near future.

The data of Meditz et al [4] also suggest that more immediate challenges lay at hand. The continued evidence of disparities in engagement in care and treatment based on race, gender, and geography is troubling, but not unexpected. In this era of “seek, test, and treat,” understanding these barriers to therapy is critically important, as appropriate interventions could have a rapid effect on disease course for significant numbers of HIV-infected individuals. This study focuses on individuals who receive appropriate HIV testing and are diagnosed in the early stages of infection, clearly a minority

population among those living with HIV. Although the seek and test portions of the formula were performed optimally, the treat component proved not to be so easy. Women, nonwhites, and those living in the Southern United States were significantly less likely to start antiretroviral therapy and were more likely to have AIDS-related complications or to have a CD4+ T cell count <200 cells/μL. Unfortunately, the authors do not present data among those who did start therapy, to assess whether racial, gender, and geographic differences persisted among patients retained in care, the critical fourth component of the spectrum of engagement in care. Response to antiretroviral therapy has not been shown to differ by gender when therapy is administered and taken appropriately [5]; however, lower rates of virologic suppression have been well documented despite similar duration of HIV infection and equal access to healthcare in the military [6], a finding that remains to be fully explained. The implication from the work by Meditz et al [4] is that socioeconomic factors are a critical influence in determining the likelihood of engaging patients in care. As a result, these factors cannot be overlooked when developing programs that aim to increase the percentage of HIV-infected

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patients on therapy with undetectable viremia.

The recently released “National HIV/AIDS Strategy” (<http://www.whitehouse.gov/sites/default/files/uploads/NHAS.pdf>) identifies 3 primary goals: (1) reducing the number of persons who become infected with HIV, (2) increasing access to care and optimizing health outcomes for people living with HIV, and (3) reducing HIV-related health disparities. The findings from this study threaten the success of each of these pillars if the socioeconomic factors leading to delayed initiation of antiretroviral therapy and poor retention in HIV care are not better understood and addressed.

Although a direct causal link between HIV acquisition or initiation of care and many socioeconomic variables has not been demonstrated, some like poverty, intimate partner violence and food insecurity are increasingly recognized as factors significantly associated with increased high-risk sexual behaviors, decreased initiation and retention in care, and worse clinical outcomes [7–9]. These are not easy challenges to solve, but they represent some of the most important social issues underlying health disparities in the United States.

Beyond these structural issues that impact HIV disparities, many other nonbiologic and potentially modifiable factors may contribute to the gender, racial, and geographic differences noted in this study. For example, there may be important differences in trust in the healthcare system among minority and vulnerable populations [10] that may

influence the worse outcomes seen in the study of Meditz et al [4]. Identifying which factors are the most significant barriers to participation in care and designing appropriate interventions are necessary to make any headway in erasing the disparities that are evident in studies like this and others.

Herein lies the challenge. Although biologic differences in HIV presentation and outcomes exist among genders and races, these are not easily altered, nor are they known to be of major clinical significance. Socioeconomic factors play a much more important role in determining HIV disease outcomes, at an individual as well as at a population level, and although theoretically modifiable, they represent complex challenges that are beyond the traditional influence of public health. A collaborative policy and research effort across all levels of community, government, and science must be undertaken if we hope to meet the goals of the National HIV/AIDS Strategy.

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