Disparities in Initiation of Combination Antiretroviral Treatment and in Virologic Suppression Among Patients in the HIV Outpatient Study, 2000–2013

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**Objectives:** The National HIV/AIDS Strategy emphasizes virologic suppression (VS) to reduce HIV incidence in the United States. We assessed temporal trends of and disparities in time to combination antiretroviral therapy (cART) initiation and HIV VS in a large demographically diverse cohort of HIV-infected patients.

**Design:** We included antiretroviral-naive HIV Outpatient Study participants from 2000 to 2013 enrolled within 6 months of their HIV diagnosis who attended ≥2 HIV care-related visits.

**Methods:** We evaluated time from HIV diagnosis to first use of cART, time from HIV diagnosis to VS, and time from first use of cART to VS. Kaplan–Meier time-to-event curves and Cox proportional hazards models were used to assess temporal trends and correlates of initiating cART and achieving HIV VS (<500 copies per milliliter).

**Results:** Among 1156 HIV Outpatient Study patients [median age, 37 years; 43.2% non-Hispanic/Latino black (NHB), 14.1% Hispanic/Latino], estimated median times from HIV diagnosis to cART initiation and from HIV diagnosis to VS both shortened by >40% during the 13.5-year study period, reaching, respectively, 2.5 and 5.4 months. In multivariable analyses, NHB patients (as compared with non-Hispanic/Latino white) and those who had injected drugs (as compared with those who did not) initiated cART in a less timely fashion. After adjusting for CD4+ cell count and viral load at cART initiation, NHB patients and those aged <30 years (compared with ≥40 years) had lower rates of VS.

**Conclusions:** Despite improvements in HIV treatment over time, patients who were NHB, younger, or used injection drugs had less favorable outcomes.

**Key Words:** HIV, disparities, continuum of care, cART

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**INTRODUCTION**

The National HIV/AIDS Strategy in the United States emphasizes the importance of virologic suppression (VS) to improve the health of HIV-infected individuals and to reduce population-level transmission of HIV infection.1 Modern combination antiretroviral therapy (cART) regimens are better tolerated and less complex than older regimens, increasing the likelihood of achieving VS. The success of HPTN 052, the HIV Prevention Trials Network randomized trial which demonstrated 96% reduction in HIV transmission with use of cART in HIV serodiscordant couples, lent support to the recommendation for universal treatment of persons with HIV infection in the United States, regardless of their CD4+ cell count.2,3 Owing to improvements in the potency and tolerability of cART and changes in US guidelines to offer treatment to all patients, HIV-infected persons in the United States have been increasingly prescribed cART and achieving VS sooner after entry into HIV care.4,6 Unfortunately, disparities in the continuum of HIV care in the United States persist and access to HIV treatment and subsequent clinical responses are not equitably distributed.7–9 For example, despite the disproportionately higher diagnosis rates of HIV infection among non-Hispanic/Latino blacks (NHBs) compared with non-Hispanic/Latino whites,10 individuals in the former group have had less access to and uptake of cART and higher rates of virologic nonsuppression.8,11–13 We sought to evaluate temporal trends in cART initiation and VS in a large and demographically diverse cohort of HIV-infected patients to investigate potential risk factors and sociodemographic disparities. Understanding sociodemographic disparities is a first step toward identifying modifiable factors for interventions to improve the continuum of care for all HIV-infected persons in the United States.

**METHODS**

The HIV Outpatient Study

The HIV Outpatient Study (HOPS) is an ongoing prospective observational cohort study of HIV-infected adults...
who have received care at any of the 9 participating HIV clinics (university-based, public, and private) in 6 US cities (Chicago, IL; Denver, CO; Stonybrook, NY; Philadelphia, PA; Tampa, FL; and Washington, DC). The HOPS, which started in 1993, is an open cohort; patients may enter the study at any time after a diagnosis of HIV infection regardless of treatment history and may leave the study at any time for any reason (eg, patient request, death, or loss to follow-up). Since its inception, the HOPS protocol has been reviewed and approved annually by the institutional review boards at the Centers for Disease Control and Prevention (Atlanta, GA) and each of the local sites. Patient data, including sociodemographic characteristics, diagnoses, antiretroviral and other treatments, and laboratory values [including CD4+ T-lymphocyte count (CD4 cell count) and plasma HIV RNA viral load (HIV VL)], were abstracted from medical charts in medical records abstraction.

Study Population
HOPS participants were included in this analysis if they were newly diagnosed with HIV during 2000–2013, joined the HOPS within 6 months of their diagnosis, were ART naive at the time of entry into HOPS, and attended at least 2 clinic visits at a participating site during the study period. Observation began at the time of HIV diagnosis and ended at the last HOPS contact, death, or June 30, 2013, whichever occurred first. We analyzed HOPS data collected during January 1, 2000, to June 30, 2013, using the HOPS data set updated through December 31, 2013, to account for any lags in medical records abstraction.

Variable Definitions
For analysis, 2 dates were of interest: date of first known cART use, defined per standard criteria, and date of first VS, defined as first documented HIV VL <500 copies per milliliter after HIV diagnosis. Patients were categorized according to their age at HIV diagnosis, grouped as <25, 25–29, 30–39, and ≥40 years. Race/ethnicity was categorized as non-Hispanic/Latino white, NHB, Hispanic/Latino, and other/unknown. Patients were further classified by whether they were a person who injects drugs (IDU). We classified HOPS participants hierarchically according to their HIV transmission risk as gay, bisexual, and other men who have sex with men (collectively referred to as MSM), followed by women with heterosexual contact, men with heterosexual contact, and other/unknown. Insurance payor was defined as the primary insurance provider at the date of HIV diagnosis or earliest recorded payor thereafter and was categorized as private (ie, private insurance, preferred provider organization, health maintenance organization, point of service), public (ie, public insurance, Medicare, Medicaid, and Ryan White/AIDS Drug Assistance Program), and other/unknown (ie, self-pay, clinical study, other, unknown). We grouped HOPS clinic sites at which patients received care as either publicly or privately funded institutions. We stratified year of HIV diagnosis as 2000–2003, 2004–2007, 2008–2010, and 2011–2013. We used the laboratory values obtained closest to and within 3 months after HIV diagnosis to classify baseline CD4 cell count and HIV VL results. Similarly, for CD4 cell count and HIV VL at cART initiation, we analyzed the value obtained closest in time up to 6 months before the start of cART.

Statistical Analyses
We calculated percentages for categorical variables and medians and interquartile ranges for continuous variables. Subgroups of patients were compared using \( \chi^2 \) tests and Wilcoxon rank sum tests as appropriate; ordinal categorical variables were analyzed using the Cochran–Armitage test for trend.

We used Kaplan–Meier time-to-event methods and Cox proportional hazards models to assess temporal trends and to identify correlates of initiating cART and of achieving viral suppression after HIV diagnosis. Observation time for the primary analyses of the timing and rates of cART initiation and VS began on the date of HIV diagnosis (termed “index” date). In the secondary analyses of rates of VS, we reset the time of origin to the date of cART initiation and adjusted for laboratory values (CD4 cell count and HIV VL) at the time of cART initiation. We used univariate Cox models to examine the statistical association of these variables with age, race/ethnicity, IDU, HIV risk group, primary insurance payor, type of institution, period of HIV diagnosis, and baseline CD4 cell count. We constructed multivariable Cox models that included all variables from the univariate analyses, regardless of their statistical significance, to facilitate comparison of model findings for cART initiation and VS and to control for residual confounding. Results from the Cox proportional hazards models are reported as hazard ratios (HRs) with associated 95% confidence intervals (CI). \( P \) values less than 0.05 were considered statistically significant. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS
The 1156 HOPS patients who met eligibility criteria had a median age of 37.0 years (interquartile range: 29.1–45.4), 74.8% were male, and the study sample was ethnically diverse: 39.0% were non-Hispanic/Latino white, 43.2% NHB, 14.1% Hispanic/Latino, and race/ethnicity was other/unknown for 3.7%; 52.4% of patients were MSM and 51.7% were privately insured (Table 1).

CD4 Cell Count at HIV Diagnosis
The median CD4 cell count at HIV diagnosis was somewhat higher in consecutive periods in the study: 284 cells per cubic millimeter in 2000–2003 compared with 337 cells per cubic millimeter in 2011–2013 (test for trend \( P = 0.064, \) not significant). The median CD4 cell count at HIV diagnosis varied markedly among patient subgroups: 177 cells per cubic millimeter for heterosexual men, 371 cells per cubic millimeter for MSM, and 314 cells per cubic millimeter for heterosexual women (\( P < 0.01 \)). NHBs and Hispanics/Latinos were diagnosed with lower CD4 cell counts than whites: median
### TABLE 1. Characteristics of HIV-Infected Patients Overall and Stratified by Whether Patients Began cART, the HOPS, 2000–2013

| Characteristic                          | Total N = 1156 | Began cART n = 926 | Did Not Begin cART n = 230 | % Total Who Began cART (80.1%) | P* |
|----------------------------------------|---------------|-------------------|---------------------------|-------------------------------|----|
| **Age at index date (yrs),† n (%)**    |               |                   |                           |                               |    |
| <25                                    | 148 (12.8)    | 105 (11.3)        | 43 (18.7)                 | 70.9                          | 0.001 |
| 25–29                                  | 168 (14.5)    | 130 (14.0)        | 38 (16.5)                 | 77.4                          |    |
| 30–39                                  | 381 (33.0)    | 307 (33.2)        | 74 (32.2)                 | 80.6                          |    |
| 40+                                    | 459 (39.7)    | 384 (41.5)        | 75 (32.6)                 | 83.7                          |    |
| **Median age (IQR)**                   | 37.0 (29.1 to 45.4) | 37.7 (29.8 to 45.7) | 34.8 (27.0 to 43.2) | 0.003 |    |
| **Sex, n (%)**                         |               |                   |                           |                               | 0.39 |
| Female                                 | 291 (25.2)    | 228 (24.6)        | 63 (27.4)                 | 78.4                          |    |
| Male                                   | 865 (74.8)    | 698 (75.4)        | 167 (72.6)                | 80.7                          |    |
| **Race/ethnicity, n (%)**              |               |                   |                           |                               | 0.026 |
| Non-Hispanic/Latino white              | 451 (39.0)    | 380 (41.0)        | 71 (30.9)                 | 84.3                          |    |
| NHB                                     | 499 (43.2)    | 383 (41.4)        | 116 (50.4)                | 76.8                          |    |
| Hispanic/Latino                        | 163 (14.1)    | 131 (14.1)        | 32 (13.9)                 | 80.4                          |    |
| Other/unknown                          | 43 (3.7)      | 32 (3.5)          | 11 (4.8)                  | 74.4                          |    |
| **IDU, n (%)**                         |               |                   |                           |                               | 0.002 |
| Yes                                    | 55 (4.8)      | 35 (3.8)          | 20 (8.7)                  | 63.6                          |    |
| No                                     | 1101 (95.2)   | 891 (96.2)        | 210 (91.3)                | 80.9                          |    |
| **HIV risk group, n (%)**              |               |                   |                           |                               | 0.11 |
| MSM                                    | 606 (52.4)    | 488 (52.7)        | 118 (51.3)                | 80.5                          |    |
| Heterosexual women                     | 265 (22.9)    | 204 (22.0)        | 61 (26.5)                 | 77.0                          |    |
| Heterosexual men                       | 202 (17.5)    | 160 (17.3)        | 42 (18.3)                 | 79.2                          |    |
| Other/unknown                          | 83 (7.2)      | 74 (8.0)          | 9 (3.9)                   | 89.2                          |    |
| **Insurance payor, n (%)**             |               |                   |                           |                               | 0.10 |
| Private                                 | 598 (51.7)    | 491 (53.0)        | 107 (46.5)                | 82.1                          |    |
| Public                                  | 393 (34.0)    | 301 (32.5)        | 92 (40.0)                 | 76.6                          |    |
| Other/unknown                           | 165 (14.3)    | 134 (14.5)        | 31 (13.5)                 | 81.2                          |    |
| **Institution, n (%)**                 |               |                   |                           |                               | 0.055 |
| Private                                 | 604 (52.2)    | 497 (53.7)        | 107 (46.5)                | 82.3                          |    |
| Public                                  | 552 (47.8)    | 429 (46.3)        | 123 (53.5)                | 77.7                          |    |
| **Period of index date,† n (%)**       |               |                   |                           |                               | 0.76 |
| 2000–2003                               | 445 (38.5)    | 342 (36.9)        | 103 (44.8)                | 76.9                          |    |
| 2004–2007                               | 362 (31.3)    | 306 (33.1)        | 56 (24.3)                 | 84.5                          |    |
| 2008–2010                               | 225 (19.5)    | 185 (20.0)        | 40 (17.4)                 | 82.2                          |    |
| 2011–2013                               | 124 (10.7)    | 93 (10.0)         | 31 (13.5)                 | 75.0                          |    |
| **Days from index date† to HOPS entry, median (IQR)** | 25 (10.5 to 50) | 23.5 (10 to 48) | 30 (12 to 62) | 0.005 |    |
| **AIDS defined at index,† n (%)**      |               |                   |                           |                               | <0.001 |
| Yes                                    | 207 (17.9)    | 193 (20.8)        | 14 (6.1)                  | 93.2                          |    |
| No                                     | 949 (82.1)    | 733 (79.2)        | 216 (93.9)                | 77.2                          |    |
| **Nadir CD4 at start of cART (cells per cubic millimeter),‡ n (%)** |               |                   |                           |                               |    |
| <50                                    | 162 (17.5)    |                  | NA                       | NA                            |    |
| 50–99                                   | 74 (8.0)      |                  | NA                       | NA                            |    |
| 100–199                                 | 140 (15.1)    |                  | NA                       | NA                            |    |
| 200–349                                 | 246 (26.6)    |                  | NA                       | NA                            |    |
| ≥350                                    | 235 (25.4)    |                  | NA                       | NA                            |    |
| Unknown                                 | 69 (7.4)      |                  | NA                       | NA                            |    |
| **Median nadir CD4 (cells per cubic millimeter)‡ (IQR)** | 233 (85 to 360) |                  | NA                       | NA                            |    |
| **CD4 count at index date (cells per cubic millimeter),‡ n (%)** |               |                   |                           |                               | <0.001 |
| <200                                    | 337 (29.2)    | 314 (33.9)        | 23 (10.0)                 | 93.2                          |    |
| 200–349                                 | 204 (17.6)    | 174 (18.8)        | 30 (13.0)                 | 85.3                          |    |

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CD4 Cell Count at cART Initiation

The median CD4 cell count at cART initiation was higher for patients diagnosed in consecutive periods of the study: 207 cells per cubic millimeter in 2000–2003, 231 cells per cubic millimeter in 2004–2007, 317 cells per cubic millimeter in 2008–2010, and 317 cells per cubic millimeter in 2011–2013 (test for trend \( P < 0.001 \)). Similarly, for the subset of patients observed to start cART in a given calendar interval, the median CD4 cell count at cART initiation was 196 cells per cubic millimeter in 2000–2003 (n = 278), 222 cells per cubic millimeter in 2004–2007 (n = 308), 317 cells per cubic millimeter in 2008–2010 (n = 225), and 321 cells per cubic millimeter in 2011–2013 (n = 115) (test for trend \( P < 0.001 \)). MSM and heterosexual women had higher CD4 cell counts at cART initiation than did heterosexual men \( (P < 0.001; \text{data not shown}); \) additionally, patients of non-Hispanic/Latino white race/ethnicity had higher CD4 cell counts than those of non-Hispanic black and Hispanic/Latino race/ethnicity \( (P < 0.001; \text{data not shown}); \) There were no statistically significant differences by IDU group for CD4 cell count at cART initiation.

Time to cART Initiation After HIV Diagnosis

Overall, 926 (80.1%) of eligible patients began cART during the study period. Compared with patients who did not, patients who started cART were older (median age 37.7 vs. 34.8 years), more frequently of non-Hispanic/Latino white race/ethnicity (41.0% vs. 30.9%), and less frequently IDU participants (3.8% vs. 8.7%). They were also more likely to have been diagnosed with AIDS at the time of their HIV diagnosis (20.8% vs. 6.1%) and to have a lower CD4 cell count (median 271 vs. 517 cells per cubic millimeter) and higher HIV VL (median 4.8 vs. 4.2 \( \log_{10} \) copies per milliliter) (Table 1; \( P < 0.05 \) for all). Patients who did vs. did not start cART during the study period did not differ significantly in terms of sex, HIV transmission risk group, insurance payor, institution, or calendar period of HIV diagnosis.

In univariate analyses, the estimated median duration from HIV diagnosis to cART initiation was progressively shorter for persons diagnosed with HIV in later calendar periods: the median time was 4.4 months for persons diagnosed in 2000–2003 and 2.5 months for persons diagnosed in 2011–2013 (log rank test \( P < 0.001 \), Fig. 1A). In univariate Cox proportional hazards models for 2000–2013, factors significantly \( (P < 0.05) \) associated with \( \text{later} \) cART initiation included age \( < 25 \) years (compared with \( \geq 40 \) years) and IDU (Table 2). However, factors significantly associated with \( \text{earlier} \) cART initiation included being a heterosexual man or belonging to other/unknown risk group (compared with MSM), being diagnosed with HIV infection in later calendar periods, and having a lower CD4 cell count at diagnosis (Table 2). After adjusting for CD4 cell count and all other variables displayed in Table 2, later cART initiation was now significant for persons of NHB race/ethnicity \( \text{[adjusted HR \( (aHR) = 0.8, 95\% \text{CI: 0.7 to 0.9}, \text{as compared with non-Hispanic/Latino white; Fig. 2A shows unadjusted curves] and IDUs \( (aHR = 0.6, 95\% \text{CI: 0.4 to 0.8, vs. non-IDU})]. \) Compared with the period 2000–2003, the likelihood of initiating cART after diagnosis increased significantly for persons diagnosed with HIV during 2004–2007 \( (aHR = 1.3, 95\% \text{CI: 1.1 to 1.5}), \) during 2008–2010 \( (aHR = 1.4, 95\% \text{CI: 1.2 to 1.7}), \) and during 2011–2013 \( (aHR = 2.0, 95\% \text{CI: 1.6 to 2.6}). \) Compared with patients whose CD4 cell count at HIV diagnosis was at least

| TABLE 1. Characterization of HIV-Infected Patients Overall and Stratified by Whether Patients Began cART, the HOPS, 2000–2013 |

| Total | Began cART | Did Not Begin cART | % Total Who Began cART (80.1%) | \( P^* \) |
|-------|------------|-------------------|------------------------------|--------|
| \( \geq 350 \) | 434 (37.5) | 302 (32.6) | 132 (57.4) | 69.6 |
| Unknown | 181 (15.7) | 136 (14.7) | 45 (19.6) | 75.1 |
| Median CD4 count (cells per cubic millimeter)\( ^\dagger \) (IQR) | 309 (115 to 517) | 271 (97 to 456) | 517 (317 to 780) | <0.001 |
| Viral load at index date (\( \log_{10} \) copies per milliliter)\( ^\ddagger \) (n (%)) | 28 (2.4) | 8 (0.9) | 20 (8.7) | 28.6 |
| <3 (but detectable) | 46 (4.0) | 27 (2.9) | 19 (8.3) | 58.7 |
| \( \geq 3 \) and <5 | 536 (46.4) | 430 (46.4) | 106 (46.1) | 80.2 |
| \( \geq 5 \) | 358 (31.0) | 318 (34.3) | 40 (17.4) | 88.8 |
| Unknown | 188 (16.3) | 143 (15.4) | 45 (19.6) | 76.1 |
| Median viral load (\( \log_{10} \) copies per milliliter)\( ^\ddagger \) (IQR) | 4.7 (4.1 to 5.3) | 4.8 (4.3 to 5.3) | 4.2 (3.1 to 4.9) | <0.001 |

\( ^* \)P values for differences in distributions (comparing patients who began cART vs. those who did not) for categorical variables are based on a \( \chi^2 \) test. \( P \) values for comparing medians are based on a 2-sided Wilcoxon rank sum test. \( P \) values for ordinal variables are obtained from a Cochran–Armitage test for trend.

\( ^\dagger \)Index date is date of HIV diagnosis.

\( ^\ddagger \)Closest date from values documented 6 months before or 3 months after date.

IQR, interquartile range; NA, not applicable.
350 cells per cubic millimeter, those diagnosed with CD4 cell count less than 200 cells per cubic millimeter (aHR = 5.0, 95% CI: 4.1 to 5.9) or 200–349 cells per cubic millimeter (aHR = 2.2, 95% CI: 1.8 to 2.7) were more likely to initiate cART more promptly after HIV diagnosis.

Achieving VS After HIV Diagnosis

Of the 1156 patients included in this analysis, 916 (79.2%) achieved VS during the study period. In univariate analyses, the median time to VS improved for those diagnosed with HIV infection in later calendar periods: it was 10.2 months for patients diagnosed in 2000–2003 and 5.4 months for patients diagnosed in 2011–2013 (log rank test $P < 0.001$, Fig. 1B). In univariate Cox proportional hazards models for 2000–2013, factors significantly ($P < 0.05$) associated with later VS were age $<$25 and 25–29 years (compared with $\geq$40 years), NHB race/ethnicity (compared with Hispanic/Latino white), and receiving care at a publicly funded institution (compared with private institutions), whereas having an HIV diagnosis in later calendar years and having lower CD4 cell count at diagnosis were associated with shorter time to VS.
Time to Initiation of cART

| Age (yrs)   | HR (95% CI) | P     | aHR (95% CI) | P     |
|-------------|-------------|-------|-------------|-------|
| <25         | 0.7 (0.6 to 0.9) | 0.008 | 0.9 (0.7 to 1.1) | 0.16 |
| 25–29       | 0.8 (0.7 to 1.0) | 0.08  | 0.9 (0.7 to 1.1) | 0.34 |
| 30–39       | 0.9 (0.8 to 1.0) | 0.17  | 0.9 (0.8 to 1.1) | 0.26 |
| ≥40         | Referent     | Referent | Referent     | Referent |

Race/ethnicity

| Non-Hispanic/Latino white | Referent | Referent |
| NHB                       | 0.9 (0.8 to 1.0) | 0.14  |
| Hispanic/Latino           | 1.1 (0.9 to 1.4) | 0.31  |
| Other/unknown             | 0.9 (0.6 to 1.3) | 0.68  |

IDU

| Yes               | 0.6 (0.4 to 0.8) | 0.004  |
| No                | Referent         | Referent |

HIV risk group

| MSM                                      | Referent | Referent |
| Heterosexual women                      | 0.9 (0.8 to 1.1) | 0.38  |
| Heterosexual men                        | 1.3 (1.1 to 1.5) | 0.007  |
| Other/unknown                           | 1.3 (1.1 to 1.7) | 0.018  |

Insurance payor

| Public                      | 1.1 (0.9 to 1.2) | 0.36  |
| Other/unknown              | 1.1 (0.9 to 1.3) | 0.27  |

Institution

| Public                      | 0.9 (0.8 to 1.1) | 0.22  |

Period of index date

| 2000–2003                  | Referent | Referent |
| 2004–2007                  | 1.2 (1.0 to 1.4) | 0.052  |
| 2008–2010                  | 1.2 (1.0 to 1.5) | 0.019  |
| 2011–2013                  | 1.6 (1.3 to 2.0) | <0.001 |

CD4 count at index date

| <200                       | 4.6 (3.9 to 5.5) | <0.001 |
| 200–349                    | 2.1 (1.7 to 2.5) | <0.001 |
| ≥350                       | Referent         | Referent |
| Unknown                    | 1.1 (0.9 to 1.3) | 0.60  |

Time to VS

| Age (yrs)   | HR (95% CI) | P     | aHR (95% CI) | P     |
|-------------|-------------|-------|-------------|-------|
| <25         | 0.7 (0.6 to 0.9) | 0.003 | 0.8 (0.6 to 1.0) | 0.037 |
| 25–29       | 0.8 (0.7 to 1.0) | 0.007 | 0.8 (0.6 to 1.0) | 0.031 |
| 30–39       | 0.9 (0.8 to 1.0) | 0.08  | 0.9 (0.8 to 1.1) | 0.19  |
| ≥40         | Referent     | Referent | Referent     | Referent |

Race/ethnicity

| Non-Hispanic/Latino white | Referent | Referent |
| NHB                       | 0.9 (0.7 to 1.0) | 0.38  |
| Hispanic/Latino           | 1.0 (0.9 to 1.3) | 0.38  |
| Other/unknown             | 1.0 (0.8 to 1.5) | 0.79  |

IDU

| Yes               | 0.5 (0.3 to 0.8) | 0.002  |
| No                | Referent         | Referent |

HIV risk group

| MSM                                      | Referent | Referent |
| Heterosexual women                      | 1.0 (0.8 to 1.2) | 0.69  |
| Heterosexual men                        | 1.1 (0.9 to 1.4) | 0.23  |
| Other/unknown                           | 1.1 (0.8 to 1.4) | 0.55  |

Insurance payor

| Public                      | 1.0 (0.9 to 1.1) | 0.71  |
| Other/unknown              | 0.9 (0.8 to 1.2) | 0.80  |

Institution

| Public                      | 0.9 (0.8 to 1.0) | 0.22  |

Period of index date

| 2000–2003                  | Referent | Referent |
| 2004–2007                  | 1.3 (1.1 to 1.5) | 0.004  |
| 2008–2010                  | 1.8 (1.5 to 2.1) | <0.001 |
| 2011–2013                  | 2.1 (1.6 to 2.7) | <0.001 |

CD4 count at index date

| <200                       | 5.0 (4.1 to 5.9) | <0.001 |
| 200–349                    | 2.2 (1.8 to 2.7) | <0.001 |
| ≥350                       | Referent         | Referent |
| Unknown                    | 1.1 (0.9 to 1.4) | 0.25  |

*HRs greater than 1 indicate earlier initiation of cART or earlier VS.
†All variables from the univariate models are included in the multivariable model.
‡Index date is the date of HIV diagnosis.

multivariable analyses, adjusting for CD4 cell count and all other variables displayed in Table 2, the factors independently associated with later VS were age <25 years (aHR = 0.8, 95% CI: 0.6 to 1.0) and 25–29 years (aHR = 0.8, 95% CI: 0.6 to 1.0) compared with ≥40 years, NHB race/ethnicity (aHR = 0.8, 95% CI: 0.7 to 1.0, as compared with Hispanic/Latino white), and receiving care at a publicly funded institution (aHR = 0.8, 95% CI: 0.7 to 1.0). Compared with the participants diagnosed in the period 2000–2003, those diagnosed in 2004–2007 (aHR = 1.3, 95% CI: 1.1 to 1.6), 2008–2010 (aHR = 2.0, 95% CI: 1.7 to 2.4), or 2011–2013 (aHR = 2.6, 95% CI: 2.0 to 3.4) achieved VL suppression more rapidly. Compared with patients diagnosed with HIV with CD4 cell count at least 350 cells per cubic millimeter, those with CD4 cell count less than 200 cells per cubic millimeter (aHR = 1.9, 95% CI: 1.6 to 2.2) or CD4 cell count 200–349 cells per cubic millimeter (aHR = 1.7, 95% CI: 1.4 to 2.0) were more likely to have a shorter time to VS.

**Achieving VS After cART Initiation**

We performed a secondary analysis by resetting the time of origin in Cox regression analyses to the date of cART initiation (instead of the date of HIV diagnosis) to assess disparities in VS among those patients who were prescribed cART. Of the 1156 patients included in our main analysis,
926 began cART; 835 of whom subsequently achieved VS during study observation.

In univariate analyses, in addition to the disparities noted in Table 2 regarding time to achieve VS by age, race/ethnicity, institution, and period of HIV diagnosis (Figs. 1B, 2B), we observed additional disparities by HIV risk group and insurance payor, whereas age was no longer significant (Table 3). In multivariable analyses, participants aged <25 years were less likely to achieve VS (aHR = 0.7, 95% CI: 0.6 to 0.9) and those aged 25–29 years (aHR = 0.8, 95% CI: 0.6 to 1.0) when compared with those aged ≥40 years and NHBs were less likely to achieve VS than non-Hispanic/Latino whites (aHR = 0.8, 95% CI: 0.7 to 1.0). The likelihood of achieving earlier VS improved over time: compared with patients diagnosed during 2000–2003, the aHR was higher for patients diagnosed in 2004–2007 (aHR = 1.2, 95% CI: 1.0 to 1.4), 2008–2010 (aHR = 1.2, 95% CI: 1.0 to 1.5), and 2011–2013 (aHR = 1.8, 95% CI: 1.4 to 2.3). Patients with HIV VL ≥5 log_{10} copies per milliliter took longer to achieve VS after cART initiation (aHR = 0.7, 95% CI: 0.6 to 0.8), compared with those having HIV VL from 3 to 5 log_{10} copies per milliliter. Neither IDU nor CD4 cell count at cART initiation was independently associated with time to VS after cART initiation.

**DISCUSSION**

In this longitudinal observational cohort of HIV-infected US patients, time to initiation of cART and time to
TABLE 3. Factors Associated With Time to VS After cART Initiation, the HOPS, 2000–2013 (n = 926)

| Time to VS*        | Univariate | Multivariable† |
|--------------------|------------|----------------|
|                    | HR (95% CI) | aHR (95% CI)   |
|                    | P          | P              |
| Age (yrs)          |            |                |
| <25                | 0.8 (0.6 to 1.0) | 0.09          | 0.7 (0.6 to 0.9) | 0.009 |
| 25–29              | 0.8 (0.7 to 1.1) | 0.13          | 0.8 (0.6 to 1.0) | 0.047 |
| 30–39              | 0.9 (0.8 to 1.1) | 0.28          | 0.9 (0.8 to 1.0) | 0.14  |
| ≥40                | Referent   | Referent       |                |
| Race/ethnicity     |            |                |
| Non-Hispanic/ Latino white | Referent | Referent       |                |
| NHB                | 0.8 (0.7 to 0.9) | 0.001         | 0.8 (0.7 to 1.0) | 0.048 |
| Hispanic/Latino    | 0.8 (0.7 to 1.0) | 0.072         | 0.9 (0.7 to 1.1) | 0.38  |
| Other/unknown      | 0.9 (0.6 to 1.3) | 0.58          | 0.8 (0.6 to 1.2) | 0.40  |
| IDU                |            |                |
| Yes                | 1.0 (0.7 to 1.4) | 0.88          | 1.0 (0.7 to 1.5) | 0.88  |
| No                 | Referent   | Referent       |                |
| HIV risk group     |            |                |
| MSM                | Referent   | Referent       |                |
| Heterosexual women | 0.8 (0.7 to 1.0) | 0.023         | 1.0 (0.8 to 1.2) | 0.90  |
| Heterosexual men   | 0.9 (0.7 to 1.1) | 0.30          | 1.1 (0.8 to 1.3) | 0.67  |
| Other/unknown      | 0.9 (0.7 to 1.2) | 0.37          | 1.0 (0.8 to 1.4) | 0.81  |
| Insurance payor    |            |                |
| Private            | Referent   | Referent       |                |
| Public             | 0.8 (0.7 to 1.0) | 0.035         | 0.9 (0.8 to 1.1) | 0.36  |
| Other/unknown      | 0.9 (0.7 to 1.1) | 0.41          | 1.0 (0.8 to 1.3) | 0.73  |
| Institution        |            |                |
| Private            | Referent   | Referent       |                |
| Public             | 0.8 (0.7 to 0.9) | 0.004         | 0.9 (0.8 to 1.1) | 0.26  |
| Period of index date‡ |          |                |
| 2000–2003          | Referent   | Referent       |                |
| 2004–2007          | 1.2 (1.1 to 1.5) | 0.010         | 1.2 (1.0 to 1.4) | 0.021 |
| 2008–2010          | 1.3 (1.1 to 1.6) | 0.002         | 1.2 (1.0 to 1.5) | 0.046 |
| 2011–2013          | 1.7 (1.3 to 2.2) | <0.001        | 1.8 (1.4 to 2.3) | <0.001 |
| CD4 at cART initiation (cells per cubic millimeter)§ |            |                |
| <200               | 0.7 (0.6 to 0.9) | <0.001        | 0.9 (0.7 to 1.0) | 0.14  |
| 200–349            | 1.1 (0.9 to 1.3) | 0.25          | 1.2 (1.0 to 1.5) | 0.07  |
| ≥350               | Referent   | Referent       |                |
| Unknown            | 0.6 (0.5 to 0.8) | <0.001        | 0.8 (0.6 to 1.2) | 0.29  |
| Log VL at cART initiation (log10 copies per milliliter)¶ |            |                |
| <3                 | 1.1 (0.7 to 1.6) | 0.77          | 1.3 (0.8 to 2.0) | 0.28  |
| ≥3 and <5          | Referent   | Referent       |                |
| ≥5                 | 0.7 (0.6 to 0.8) | <0.001        | 0.7 (0.6 to 0.8) | <0.001 |
| Unknown            | 0.5 (0.4 to 0.7) | <0.001        | 0.6 (0.5 to 0.8) | 0.001 |

*HRs greater than 1 indicate earlier initiation of cART or earlier VS, based on Cox proportional hazards models.
†All variables from the univariate models are included in the multivariable model.
‡Index date is the date of HIV diagnosis.
§Closest laboratory value to cART initiation up to 6 months before.

VS have improved markedly during 2000–2013 for patients who entered HIV care within 6 months after their diagnosis. Our results are similar to earlier findings from a large North American AIDS Cohort Collaboration on Research and Design6 and somewhat exceed the estimates from the National HIV Surveillance System, which reported that among persons diagnosed with HIV infection in 2009 who entered care within the next 3 months, the median time from HIV diagnosis to viral suppression was approximately 11 months.3

In the present report and in an earlier HOPS analysis through year 2009,16 there were no statistically significant improvements over the years in CD4 cell counts at the time of HIV diagnosis. However, in the current analysis, we found a significant increase in CD4 counts at the time of cART initiation. From the vantage point of our analysis cohort, which includes only persons who successfully linked to HIV care at HOPS clinics, once patients were diagnosed and in HIV care, they initiated therapy increasingly more promptly, a finding consistent with changes in treatment guidelines recommending that treatment be offered to all patients regardless of CD4 cell count.2 As a result of earlier cART initiation and likely improvements in potency and tolerability of cART over time, we observed more prompt VS after HIV diagnosis across the study intervals.

Despite overall improvements, we found that some patient subgroups lagged behind others in initiating cART and achieving VS, as has been shown in other populations.5,12 Most notably, NHBs experienced delays in initiating cART as compared with non-Hispanic/Latino whites even after controlling for public insurance payor (a surrogate indicator of poverty) and being enrolled at publicly funded sites; both variables have been shown to be associated with poorer outcomes in the HOPS cohort.15,16 The association of NHB race with later initiation of cART may stem from residual confounding by poverty, access to HIV care, or other structural or psychosocial factors that were not captured by our medical abstraction study.6 Other studies addressing racial disparities in cART initiation or discontinuation included stigma, fear of disclosure,17 distrust of the medical establishment or providers,18–20 low literacy,24 poor access to care management,25 and racial/ethnic discrimination26,27 as contributing factors. Other factors associated with poverty, including living in high-crime neighborhoods and substance abuse, may also contribute to delayed access to effective care.28 The health impact of incarceration and subsequent barriers to reentry into society are not only difficult to measure but also likely affect access to HIV care.29

Heterosexual women were diagnosed with HIV at lower CD4 cell counts than MSM but did not experience delays in initiating cART and did not lag behind MSM in time to VS, in contrast to findings by others.1,21 Of note, HIV among heterosexual men had significantly lower median CD4 counts at diagnosis compared with other risk groups, but once diagnosed, they initiated CART and achieved VS no later than MSM (Table 2). Later diagnosis among heterosexual men vs. MSM echoes findings from some European countries, which differ demographically from the United States.30,31 A recent study from Florida also observed that heterosexual men were
being diagnosed late (i.e., at lower CD4 cell counts) in rural compared with urban settings. Unlike the Florida study, the HOPS cohort is based in urban US settings. Heterosexual men may not perceive themselves at risk for HIV infection and therefore may not seek HIV testing, but just as heterosexual women are at risk, their heterosexual male counterparts are no less so.

Perhaps, the most important finding from the current analysis was the age-related disparities, with patients <25 years at HIV diagnosis or cART initiation and marked delays in achieving VS compared with patients ≥40 years, even after adjusting for CD4 cell counts and calendar year of HIV diagnosis. The incidence rate of new HIV infections has been increasing most rapidly among young adults, which is also the group with the greatest delays in accessing HIV care and poorest adherence to ART and VS. Among the estimated 47,500 new HIV infections in the United States in 2010, about 29,800 (or 63%) occurred among MSM, of whom about 36% were NHB and 30% were 13–24 years old. Nonadherence to treatment among youth is not unique to HIV and has been reported with other chronic illnesses. Youth with HIV have poorer access to care, adherence to medication, and retention in care than adults (reviewed in Zanoni and Mayer). Our study has some limitations. We studied patients who were linked to HIV care and enrolled in the HOPS study within 6 months of their HIV diagnosis; thus, our findings may reflect more favorable patterns in cART initiation and viral suppression than would be observed for all HIV-infected patients in the United States, an estimated 23% of whom do not promptly enter HIV care after being diagnosed. We relied on routinely abstracted medical records data and did not capture information on some potential structural and psychological confounders, as noted above. Measurements of HIV viral load were conducted as part of routine HIV care, and because the schedule of viral load monitoring may vary by physician practice and individual patient’s adherence to clinical visits, we may have overestimated the median times to VS. The delay to VS after controlling for time to cART start could well reflect poor adherence to prescribed cART, which we did not have data to evaluate in this study. Failure to suppress HIV VL highly correlates with nonadherence. Finally, we did not have available data on some patient-level risk factors for delayed cART start or adherence to care and cART, such as depression or alcohol dependence, or structural and socioeconomic factors as income, housing instability, or stigma and discrimination that could interfere with achieving optimal outcomes.

In conclusion, we found that over a 13.5-year period (2000–2013), although the CD4 count at HIV diagnosis has not improved significantly among enrollees in the HOPS, the timeliness of initiation of cART and subsequent VS have both improved. However, heterosexual men were diagnosed at significantly lower CD4 counts than all other subgroups. NHBS initiated treatment and achieved VS significantly later than all other subgroups. Young people aged <25 years also experienced significantly later VS compared with persons aged ≥40 years. These observations highlight the disparities that persist within the US continuum of HIV care that must be adequately addressed as part of the National HIV/AIDS Strategy.

REFERENCES
1. Office of National AIDS Policy. National HIV/AIDS Strategy for the United States. Available at: http://aids.gov/federal-resources/national-hiv-aids-strategy/nhas.pdf. Accessed June 20, 2014, 2010.
2. DHHS. Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents. Available at: http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf. Accessed June 20, 2014, 2012.
3. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493–505.
4. Hall HI, Tang T, Westfall AO, et al. HIV care visits and time to viral suppression, 19 U.S. jurisdictions, and implications for treatment, prevention and the national HIV/AIDS strategy. PLoS One. 2013;8: e69318.
5. Hoots B, Finlayson T, Weinert C, et al. Early Linkage to HIV Care and Antiretroviral Therapy Use Among MSM — 20 US Cities, 2008 and 2011. In: Conference on Retroviruses and Opportunistic Infections. Boston, MA; March 3–6, 2014.
6. Johnson DB, Buchacz K, Gebo KA, et al. Trends and disparities in antiretroviral therapy initiation and virologic suppression among newly treatment-eligible HIV-infected individuals in North America, 2001–2009. Clin Infect Dis. 2013;56:1174–1182.
7. Althoff KN, Rebeiro P, Brooks JT, et al. Disparities in the quality of HIV care when using US Department of Health and Human Services indicators. Clin Infect Dis. 2014;58:1185–1189.
8. Office of National AIDS Policy. National HIV/AIDS Strategy: Improving Outcomes: Accelerating Progress Along the HIV Care Continuum. Available at: http://www.whitehouse.gov/sites/default/files/onap_nhas_improving_outcomes_dec_2013.pdf. Accessed June 20, 2014, 2013.
9. Valdiserri RO, Forsyth AD, Yakovchenko V, et al. Measuring what matters: development of standard HIV core indicators across the U.S. Department of health and human services. Public Health Rep. 2013;128: 354–359.
10. MMWR. Disparities in diagnoses of HIV infection between blacks/African Americans and other racial/ethnic populations–37 states, 2005-2008. MMWR Morb Mortal Wkly Rep. 2011;60:93–98.
11. Oster AM, Wiegand RE, Sionean C, et al. Understanding disparities in HIV infection between black and white MSM in the United States. AIDS. 2011;25:1103–1112.
12. Agwu AL, Fleishman JA, Korthuis PT, et al. Disparities in antiretroviral treatment: a comparison of behaviorally HIV-infected youth and adults in the HIV Research Network. J Acquir Immune Defic Syndr. 2011;58:1010–1017.
13. Hall HI, Byers RH, Ling Q, et al. Racial/ethnic and age disparities in HIV prevalence and disease progression among men who have sex with men in the United States. Am J Public Health. 2007;97:1060–1066.
14. Mooman AC, Holmberg SD, Marlowe SJ, et al. Changing conditions and treatments in a dynamic cohort of ambulatory HIV patients: the HIV outpatient study (HOPS). Ann Epidemiol. 1999;9:349–357.
15. Palella FJ Jr, Baker RK, Buchacz K, et al. Increased mortality among publicly insured participants in the HIV Outpatient Study despite HAART treatment. AIDS. 2011;25:1865–1876.
16. Buchacz K, Aron C, Palella FJ, et al. CD4 cell counts at HIV diagnosis among HIV outpatient study participants, 2000–2009. AIDS Res Treat. 2012;2012:869841.
17. Mathew MO, Chesney MA, Neilands TB, et al. Disparities in reported reasons for not initiating or stopping antiretroviral treatment among a diverse sample of persons living with HIV. J Gen Intern Med. 2009;24: 247–251.
18. Schneider J, Kaplan SH, Greenfield S, et al. Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection. J Gen Intern Med. 2004; 19:1096–1103.
19. Blackstock OI, Addison DN, Brennan JS, et al. Trust in primary care providers and antiretroviral adherence in an urban HIV clinic. J Health Care Poor Underserved. 2012;23:88–98.
20. Bogart LM, Thorburn S. Are HIV/AIDS conspiracy beliefs a barrier to HIV prevention among African Americans? J Acquir Immune Defic Syndr. 2005;38:213–218.
21. Graham JL, Grimes RM, Slomka J, et al. The role of trust in delayed HIV diagnosis in a diverse, urban population. *AIDS Behav.* 2013;17:266–273.

22. Saha S, Jacobs EA, Moore RD, et al. Trust in physicians and racial disparities in HIV care. *AIDS Patient Care STDS.* 2010;24:415–420.

23. Whetten K, Leserman J, Whetten R, et al. Exploring lack of trust in care providers and the government as a barrier to health service use. *Am J Public Health.* 2006;96:716–721.

24. Osborn CY, Paasche-Orlow MK, Davis TC, et al. Health literacy: an overlooked factor in understanding HIV health disparities. *Am J Prev Med.* 2007;33:374–378.

25. Katz MH, Cunningham WE, Fleishman JA, et al. Effect of case management on unmet needs and utilization of medical care and medications among HIV-infected persons. *Ann Intern Med.* 2001;135:557–565.

26. Mugavero MJ, Lin HY, Allison JJ, et al. Racial disparities in HIV virologic failure: do missed visits matter? *J Acquir Immune Defic Syndr.* 2009;50:100–108.

27. Thrasher AD, Earp JA, Golin CE, et al. Discrimination, distrust, and racial/ethnic disparities in antiretroviral therapy adherence among a national sample of HIV-infected patients. *J Acquir Immune Defic Syndr.* 2008;49:84–93.

28. Smith KY. Paying the price for late starts and early stops: racial and sex disparities in HIV-related mortality. *Clin Infect Dis.* 2009;49:1579–1581.

29. Alexander M. *The New Jim Crow: Mass Incarceration in the Age of Colorblindness.* Jackson, Tenn: New Press, New York, NY; Distributed by Perseus distribution; 2010.

30. Delpierre C, Cuzin L, Lauwers-Cances V, et al. High-risk groups for late diagnosis of HIV infection: a need for rethinking testing policy in the general population. *AIDS Patient Care STDS.* 2006;20:838–847.

31. Buetikofer S, Wandeler G, Kouyos R, et al. Prevalence and risk factors of late presentation for HIV diagnosis and care in a tertiary referral centre in Switzerland. *Swiss Med Wkly.* 2014;144:w13961.

32. Trepka MJ, Fennie KP, Sheehan DM, et al. Late HIV diagnosis: differences by rural/urban residence, Florida, 2007-2011. *AIDS Patient Care STDS.* 2014;28:188–197.

33. CDC. Estimated HIV incidence in the United States, 2007-2010. *HIV Surveillance Suppl Rep.* 2012;17:1–26.

34. Centers for Disease Control and Prevention. HIV Surveillance Report, 2011; 23. http://www.cdc.gov/hiv/topics/surveillance/resources/reports/. Published February 2013.

35. Bradley H, Hall HI, Woltziki RJ, et al. Vital Signs: HIV diagnosis, care, and treatment among persons living with HIV–United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2014;63:1113–1117.

36. Kyser M, Buchacz K, Bush TJ, et al. Factors associated with non-adherence to antiretroviral therapy in the SUN study. *AIDS Care.* 2011; 23:601–611.

37. Bryden KS, Dunger DB, Mayou RA, et al. Poor prognosis of young adults with type 1 diabetes: a longitudinal study. *Diabetes Care.* 2003;26:1052–1057.

38. Zanoni BC, Mayer KH. The adolescent and young adult HIV cascade of care in the United States: exaggerated health disparities. *AIDS Patient Care STDS.* 2014;28:128–135.

39. Cohen SM, VanHandel MM, Branson BM, et al. Vital Signs: HIV prevention through care and treatment–United States. *MMWR Morb Mortal Wkly Rep.* 2011;60:1618–1623.

40. Tedaldi EM, Richardson JT, Debes R, et al. Retention in care within 1 Year of Initial HIV care visit in a Multisite US cohort: Who’s in and Who’s Out? *J Int Assoc Provid AIDS Care.* 2014;13:232–241.

41. Casado JL, Sabido R, Perez-Elias MJ, et al. Percentage of adherence correlates with the risk of protease inhibitor (PI) treatment failure in HIV-infected patients. *Antivir Ther.* 1999;4:157–161.

42. Beer L, Valverde EE, Raitford JL, et al. Clinician Perspectives on delaying initiation of antiretroviral therapy for clinically eligible HIV-infected patients. *J Int Assoc Provid AIDS Care.* 2014;1–10.

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