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BRIEF REPORT

CD4 Count at Entry into Care and at Antiretroviral Therapy Prescription among Adults with Human Immunodeficiency Virus in the United States, 2005-2018

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From 2005 to 2018, among 32013 adults with human immunodeficiency virus entering care, median time to antiretroviral therapy (ART) prescription declined from 69 to 6 days, CD4 count at entry into care increased from 300 to 362 cells/μL, and CD4 count at ART prescription increased from 160 to 364 cells/μL.

Keywords. HIV; CD4 count; antiretroviral therapy; universal treatment; treat all.

Effective antiretroviral therapy (ART) has considerably reduced morbidity and mortality in people with human immunodeficiency virus (PWH). In the early years of ART, public health agencies recommended that CD4 count be used for timing ART initiation in the absence of an AIDS-defining illness. Due to toxicity, resistance, and adherence concerns with early ART agents, treatment for asymptomatic patients would be deferred until CD4 counts dropped below recommended thresholds. With improvements in potency and tolerability and evidence that supports early ART initiation [1], CD4 count thresholds in treatment guidelines issued by the US Department of Health and Human Services (DHHS) steadily increased from <200 cells/μL in 2001 to <350 cells/μL in 2007 to 350–500 cells/μL in 2009 [2]. In March 2012, the DHHS revised treatment guidelines to recommend therapy for all PWH regardless of CD4 count, commencing the era of "treat all" [2]. The World Health Organization adopted the same recommendation in 2015 [3].

Within the context of these evolving treatment guidelines, we expected to observe reduced time from entry into care to prescription of ART and subsequent increases in CD4 counts at ART prescription. Using observational data from the largest cohort collaboration of PWH in North America, we describe trends in time from entry into care to ART prescription and CD4 count at both milestones between 2005 and 2018.

METHODS

Study Population

The North American AIDS Cohort Collaboration on Research and Design [4] (NA-ACCORD) is a collaboration of more than 20 clinical and interval cohort studies comprising nearly 200 000 PWH in the United States and Canada, and a regional representative of the International Epidemiology Databases to Evaluate AIDS. NA-ACCORD participants have been shown to be demographically similar to PWH in the United State, as captured by the National HIV Surveillance System of the US Centers for Disease Control and Prevention [5].

Participants of clinical cohort studies who attend 2 or more HIV clinic visits within 12 months are eligible for enrollment in the NA-ACCORD. NA-ACCORD participants provide informed consent or contributed data with a waiver of informed consent where approved by local institutional review boards. Clinical data are primarily sourced from point-of-care electronic medical records.

A total of 95 415 adults aged ≥18 years enrolled in the NA-ACCORD between 1 January 2005 and 31 December 2018. Because our focus was the impact of DHHS universal treatment guidelines on PWH engaged in clinical care in the United States, we excluded adults enrolled in study cohorts prior to the cohorts joining the NA-ACCORD [6] (n = 531), studies in Canada (n = 4998), and interval cohort studies (which are not based in clinical practice; n = 5093). Participants with no CD4 count measurement at entry into care (n = 12939), medical records that suggest participants were ART-experienced (history of ART prescription or viral load measurement <500 copies/mL prior to entering care; n = 39253), or previous AIDS diagnosis (n = 588) were also excluded.

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The total study population comprised 32 013 participants who entered care with a CD4 count measurement. This sample was used to calculate median CD4 count at entry into care. Of the total sample, 26 555 (83%) were prescribed ART during the study period with a CD4 count measurement at ART prescription. This subsample was used to calculate median CD4 count at ART prescription and time from entry into care to ART prescription.

Outcome Assessment

Time from entry into care to ART prescription was defined as the number of days between the first HIV care visit and the first ART prescription. CD4 count at entry into care (–90/+30 days) and ART prescription (–90/+30 days) were expressed as the number of CD4+ T lymphocytes per microliter of whole blood (cells/μL). For participants who had >1 CD4 count measurement within the 120-day window, we used the measurement that was collected closest to the date of entry into care/ART prescription. If ART was prescribed on the same date as entry into care, we used the same CD4 count measurement for both dates. We defined ART as a treatment regimen that included a protease inhibitor, nonnucleoside reverse transcriptase inhibitor, and/or integrase strand transfer inhibitor.

Statistical Analyses

We calculated median (interquartile range [IQR]) days from entry into care to ART prescription by year of ART prescription. We calculated median (IQR) CD4 count at entry into care by year of entry into care. We calculated median (IQR) CD4 count at ART prescription by year of ART prescription. Additionally, we calculated the above measures stratified by sex, race/ethnicity, injection drug use (IDU), and geographic region of residence.

RESULTS

Of 32 013 study participants, 26 844 (84%) were men and 5169 (16%) were women; 208 identified as transgender. A total of 14 378 (45%) participants were Black, 10 470 (33%) were White, 5002 (16%) were Hispanic (any race), 694 (2%) were Asian/Pacific Islanders, 140 (0.4%) were Indigenous, 87 (0.3%) were multiracial, and 1242 (4%) were of unknown race/ethnicity. A total of 14 032 (44%) reported male-to-male sexual contact, and 3615 (11%) reported IDU. Median age was 39 years (IQR, 29–49).

Median time from entry into care to ART prescription declined over the study period (Figure 1, Supplementary Material). Median days from entry into care to ART prescription was 69 (IQR, 20–544) in 2005, 29 (IQR, 11–73) in 2012 (the year DHHS released universal treatment guidelines), and 6 (IQR, 0–16) in 2018. In 2018, 35% of participants who entered HIV care were prescribed ART the same day.

Median CD4 count at entry into care increased from 2005 to 2011 and then remained generally stable through 2018 (Figure 1, Supplementary Material). Median CD4 count at entry into care was 300 cells/μL (IQR, 112–480) in 2005, 359 cells/μL (IQR, 171–542) in 2012, and 362 cells/μL (IQR: 189–534) in 2018.

Median CD4 count at ART prescription increased from 2005 to 2013 and remained generally stable through 2018 (Figure 1, Supplementary Material). Median CD4 count at ART

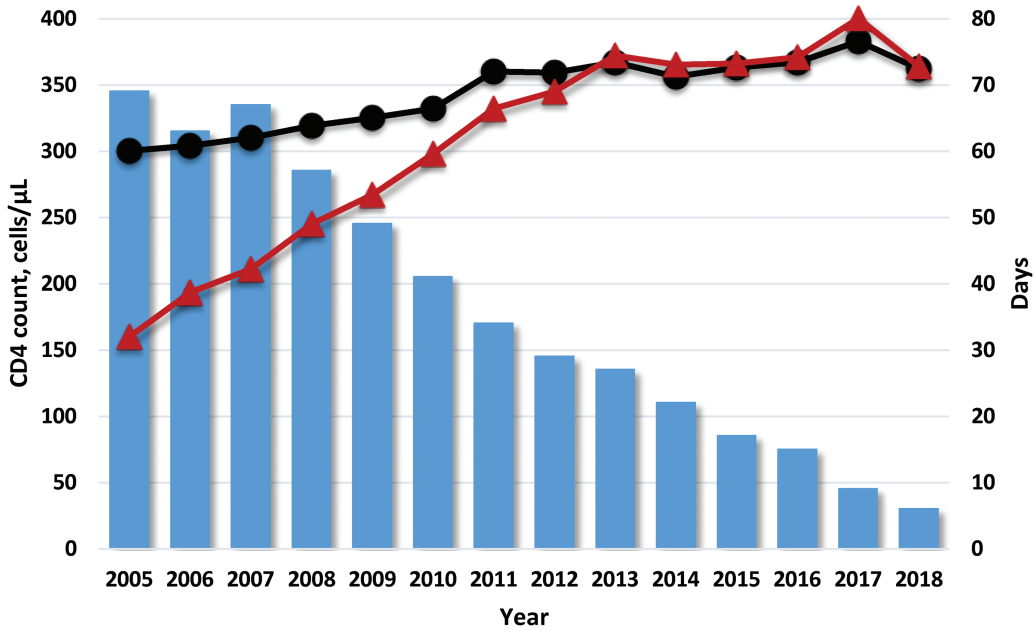

Figure 1. Median CD4 count at entry into care (black circles) and at antiretroviral therapy (ART) prescription (red triangles) overlaying median days from entry into care to ART prescription (blue bars) by calendar year.

prescription was 160 cells/μL (IQR, 51–291) in 2005, 345 cells/μL (IQR, 177–504) in 2012, and 364 cells/μL (IQR, 187–541) in 2018.

Median time from entry into care to ART prescription declined and median CD4 count at both time points increased over the study period in all subgroups (we note limited numbers of participants living in the Midwest in the latter years of the study period; Supplementary Material). For the majority of the study period, participants of non-White race and living in the South had lower median CD4 counts at entry into care and at ART prescription than participants who were White and living in other regions of the United States, respectively. Median CD4 counts at entry into care and at ART prescription were similar over time by sex and IDU status. Early in the study period, median time to ART prescription was higher in women and participants with a history of IDU than in men and participants with no IDU history, respectively. There were no notable disparities in median time to ART prescription after 2009.

DISCUSSION

Time from entry into HIV care to ART prescription has substantially shortened throughout the modern ART era, reflecting evidence that supports early ART initiation, evolving treatment guidelines, and adoption of "treat all" in clinical practice. In this descriptive study of NA-ACCORD participants, median time from entry into care to ART prescription declined from more than 3 months in 2005 to less than 1 week in 2018.

We observed a slight increase in median CD4 count at entry into HIV care over the study period, indicating modest progress toward earlier diagnosis and referral to care, which is critical for reaching 90–90–90 targets and ending the HIV epidemic [7, 8]. A significant proportion of participants entered into care with CD4 counts <350 cells/μL throughout the study period, which suggests continued challenges with HIV screening and may have implications for policy and programming that promote expanded testing and efficient linkage to care. We observed a more apparent increase in median CD4 count at ART prescription over the study period, which was expected with changing treatment guidelines. In our study population, the gap between median CD4 count at entry into care and at ART prescription had been narrowing since 2005, and there was little difference between median CD4 counts at the 2 time points after 2012, likely due to implementation of universal treatment initiation practices [9].

We note that this study used data collected during the course of clinical care and not primarily for research purposes. We observed a lower number of eligible study participants who entered care and received ART prescriptions in the latter years of the study period than in earlier years, likely due to data reporting lags, though we do not expect that this impacted our overall findings. Additionally, due to NA-ACCORD eligibility criteria, participants of this study were restricted to adults engaged in HIV care. Compared with all people diagnosed with HIV in the United States, the NA-ACCORD enrolls a higher proportion of men and participants of White race. Women and people of color are more likely to face structural barriers to HIV care [10–12], which may impact the generalizability of our findings.

These findings indicate progress toward prompt diagnosis, referral to care, and ART prescription in PWH in the United States between 2005 and 2018. Further increases in median CD4 count at both entry into care and at ART prescription may be possible with expanded implementation of effective test-and-treat strategies, particularly those that focus on reaching women, racial and ethnic minorities, and other marginalized populations disproportionately affected by HIV.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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