Association of Race and Ethnicity With Initial Prescription of Antiretroviral Therapy Among People With HIV in the US

Lauren C. Zalla, PhD; Stephen R. Cole, PhD; Joseph J. Eron, MD; Adaora A. Adimora, MD, MPH; Anissa I. Vines, MS, PhD; Keri N. Althoff, MPH, PhD; Michael J. Silverberg, PhD, MPH; Michael A. Horberg, MD, MAS; Vincent C. Marconi, MD; Sally B. Coburn, PhD, MPH; Raynell Lang, MD, MS; Emily C. Williams, PhD, MPH; M. John Gill, MBChB; Kelly A. Gebo, MD, MPH; Marina Klein, MD, MS; Timothy R. Sterling, MD; Peter F. Rebeiro, PhD, MHS; Angel M. Mayor, MD, MS; Richard D. Moore, MD; Jessie K. Edwards, PhD

IMPORTANCE Integrase strand transfer inhibitor (INSTI)–containing antiretroviral therapy (ART) is currently the guideline-recommended first-line treatment for HIV. Delayed prescription of INSTI-containing ART may amplify differences and inequities in health outcomes.

OBJECTIVES To estimate racial and ethnic differences in the prescription of INSTI-containing ART among adults newly entering HIV care in the US and to examine variation in these differences over time in relation to changes in treatment guidelines.

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational study of 42 841 adults entering HIV care from October 12, 2007, when the first INSTI was approved by the US Food and Drug Administration, to April 30, 2019, at more than 200 clinical sites contributing to the North American AIDS Cohort Collaboration on Research and Design.

EXPOSURES Combined race and ethnicity as reported in patient medical records.

MAIN OUTCOMES AND MEASURES Probability of initial prescription of ART within 1 month of care entry and probability of being prescribed INSTI-containing ART. Differences among non-Hispanic Black and Hispanic patients compared with non-Hispanic White patients were estimated by calendar year and time period in relation to changes in national guidelines on the timing of treatment initiation and recommended initial treatment regimens.

RESULTS Of 41 263 patients with information on race and ethnicity, 19 378 (47%) as non-Hispanic Black, 6798 (16%) identified as Hispanic, and 13 539 (33%) as non-Hispanic White; 36 394 patients (85%) were male, and the median age was 42 years (IQR, 30 to 51). From 2007-2015, when guidelines recommended treatment initiation based on CD4+ cell count, the probability of ART initiation within 1 month of care entry was 45% among White patients, 45% among Black patients (difference, 0% [95% CI, −1% to 1%]), and 51% among Hispanic patients (difference, 5% [95% CI, 4% to 7%]). From 2016-2019, when guidelines strongly recommended treating all patients regardless of CD4+ cell count, this probability increased to 66% among White patients, 68% among Black patients (difference, 2% [95% CI, −1% to 5%]), and 71% among Hispanic patients (difference, 5% [95% CI, 1% to 9%]). INSTIs were prescribed to 22% of White patients and only 17% of Black patients (difference, −5% [95% CI, −7% to −4%]) and 17% of Hispanic patients (difference, −5% [95% CI, −7% to −3%]) from 2009-2014, when INSTIs were approved as initial therapy but were not yet guideline recommended. Significant differences persisted for Black patients (difference, −6% [95% CI, −8% to −4%]) but not for Hispanic patients (difference, −1% [95% CI, −4% to 2%]) compared with White patients from 2014-2017, when INSTI-containing ART was a guideline-recommended option for initial therapy; differences by race and ethnicity were not statistically significant from 2017-2019, when INSTI-containing ART was the single recommended initial therapy for most people with HIV.

CONCLUSIONS AND RELEVANCE Among adults entering HIV care within a large US research consortium from 2007-2019, the 1-month probability of ART prescription was not significantly different across most races and ethnicities, although Black and Hispanic patients were significantly less likely than White patients to receive INSTI-containing ART in earlier time periods but not after INSTIs became guideline-recommended initial therapy for most people with HIV. Additional research is needed to understand the underlying racial and ethnic differences and whether the differences in prescribing were associated with clinical outcomes.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Lauren Zalla, PhD, Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, 615 N Wolfe St, Room W6508, Baltimore, MD 21205 (lzalla1@jhu.edu).

Improvements in HIV treatment since the early 1980s have led to increased life expectancy among people with HIV.[1] Major advances include the introduction of combination antiretroviral therapy (ART) and most recently, the development of integrase strand transfer inhibitors (INSTIs). First approved in 2007, INSTIs are a class of antiviral drugs that block the action of integrase, an enzyme that facilitates viral replication. Treatment with INSTI-containing ART has been associated with more rapid viral suppression, fewer adverse effects, and decreased risk of virologic failure and resistance selection compared with treatment using non-INSTI-containing ART,[2-6] and it is currently the standard of care for patients initiating ART in the US.[7] Few studies have examined racial and ethnic disparities in INSTI prescription, despite well-documented disparities in the prescription of earlier forms of ART.[8-10] Disparities in the timely prescription of INSTI-containing ART are likely to exacerbate existing inequities in viral suppression[11,12] and mortality[13,14] among people with HIV.

This study examined racial and ethnic differences in the timely prescription of INSTI-containing ART among US adults newly entering HIV care after the first INSTI was approved by the US Food and Drug Administration (FDA) on October 12, 2007, including differences in time from care entry to ART prescription and in the probability of being prescribed INSTI-containing ART. Analyses were stratified by calendar year and time period to examine variation in racial and ethnic differences over time, with time periods defined in relation to key changes in national treatment guidelines.

Key Points

Questions Did antiretroviral therapy (ART) prescriptions differ by race and ethnicity among people entering HIV care in the US from 2007-2019?

Findings In this retrospective observational study that included 42 841 individuals entering HIV care, the 1-month probability of ART prescription was not significantly different across most race and ethnicity comparisons. However, Black and Hispanic individuals were significantly less likely than White individuals to receive prescriptions for integrase strand transfer inhibitor (INSTI)–containing ART in earlier time periods but not in later time periods once INSTIs became guideline-recommended therapy.

Meaning Among people entering HIV care within a large research consortium in the US from 2007-2019, there were differences in prescription of INSTI-containing ART by race and ethnicity in earlier time periods but not in later periods, when INSTIs were the guideline-recommended initial treatment for HIV.

Methods

Study Design

Data were obtained from the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), the largest consortium of cohorts enrolling people in HIV care in the US.[15] Cohorts represented geographic clusters of clinical sites as well as managed care consortiums and observational cohort studies (full list available elsewhere).[16] Cohorts provided standardized individual data about demographic characteristics, medications, diagnoses, laboratory values, and vital status to the central Data Management Core (University of Washington, Seattle); additional quality checks were performed by the Epidemiology/Biostatistics Core (Johns Hopkins University, Baltimore, Maryland). To enroll in NA-ACCORD, individuals must have attended at least 2 HIV care visits within 12 months; thus, study participants represented the population of US adults successfully linked to HIV care. This human subjects' research was approved by the institutional review boards of participating cohorts, the Johns Hopkins University School of Medicine, and the University of North Carolina at Chapel Hill. All study participants provided written or oral consent to secondary analysis of their deidentified health records or else had consent waived for use of fully anonymized data by local institutional review boards.

Participants

Study participants included adults (≥18 years) who were newly linked to HIV care at NA-ACCORD sites in the US from October 12, 2007 to April 30, 2019. The US participants in NA-ACCORD have similar age, sex, and racial and ethnic distributions as the broader population of persons with HIV, as captured by the National HIV Surveillance System of the US Centers for Disease Control and Prevention.[17] Participants were considered newly linked to care if they enrolled during their site's observation window (eFigure 1 in Supplement 1); did not initiate ART more than 30 days prior to enrollment; did not have any CD4+ cell measurement, viral load measurement, or AIDS-defining illness diagnosis more than 1 year prior to enrollment; and did not have any measurement showing undetectable HIV viral load any time before or up to 7 days after enrollment.

Measures

Demographic and clinical data were abstracted from medical records. Information about race and ethnicity was collected from patients as part of routine clinical care using fixed categories that differed by site; responses were harmonized by NA-ACCORD, as described in the eAppendix in Supplement 1.

The primary exposure variable for this study was combined race and ethnicity: Hispanic, non-Hispanic Black, or non-Hispanic White. A small number of participants reported non-Hispanic Asian, non-Hispanic Indigenous, or other race or ethnicity; supplemental results for these groups are presented in eTable 1 in Supplement 1. Missing data on race and ethnicity, which may be informative with respect to study outcomes, were addressed using the following procedure: first, patients with reported race but unreported ethnicity were assumed to be non-Hispanic; second, multiple imputation by chained equations was used to account for unreported race (additional details are provided in the eAppendix in Supplement 1).

Additional covariates included date of death (obtained through participating cohorts' regular queries of medical records and local, state, and federal death registries), sex assigned at birth (male or female), cohort, insurance type (public, private, or self-pay), geographic region of residence (Northeast/Mid-Atlantic, South, Midwest, or West/North Central), residence in a state that adopted and implemented Medicaid expansion by 2019, and additional variables used to impute missing race and ethnicity including year at care entry, age, gender identity, mental illness diagnosis, at-risk alcohol use, whether the patient was male and had sex with men, whether the patient used injection drugs, CD4+ cells/μL at care entry, and racial and ethnic composition of the patient's county of residence. Data regarding county racial and ethnic composition were merged with patient data by zip code of residence at care entry, as described by Edwards et al.[1]

Outcomes

The outcomes of interest were date of initial prescription of combination ART and type of initial regimen prescribed, classified as INSTI-containing vs non-INSTI-containing ART.

Statistical Analysis

Patients received follow-up from care entry until ART prescription, death, loss to follow-up (13 months with no clinic visit), cohort close, or study end on April 30, 2019. The probability of ART prescription was estimated over time since care entry, using the Aalen-Johansen estimator[18] to account for the competing risks of loss to follow-up and death. Loss to follow-up was treated as a competing risk to conservatively estimate the probability of ART prescription among patients entering care in NA-ACCORD, assuming that none of those lost to follow-up were later prescribed ART. In a supplemental analysis, the stacked risks of loss to follow-up and ART prescription were estimated; the sum of these risks represents an upper bound on the probability of ART prescription (eFigure 2 in Supplement 1). Absolute racial and ethnic differences in the 1-month probability of ART prescription were estimated for Black and Hispanic patients relative to White patients, who are historically advantaged in the context of HIV care.[19] Two-sided 95% CIs around racial and ethnic differences were estimated using the delta method[20]; intervals that exclude 0 represent evidence of a statistically significant difference at an α threshold of .05.

Among patients ever observed to start ART, the probability of being prescribed INSTI-containing initial ART (vs non-INSTI-containing initial ART) was estimated for each racial and ethnic group, and absolute differences were estimated for Black and Hispanic patients relative to White patients. Two-sided 95% CIs were estimated around probabilities based on the normal approximation to the binomial distribution and around differences in probabilities using the delta method.

When examining time to initial ART prescription, analyses were stratified by time period at care entry—before vs after the US Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (the DHHS Panel) strongly recommended ART initiation regardless of CD4+ cell count on January 28, 2016 (ie, before vs during the *treat all* era). When examining the type of initial regimen prescribed, analyses were stratified by calendar year at treatment initiation and separately by time period at treatment initiation: INSTIs approved by the FDA as salvage therapy (October 12, 2007-July 7, 2009); INSTIs approved by the FDA as initial therapy (July 8, 2009-April 30, 2014); INSTI-containing ART recommended by the DHHS Panel as an option for initial therapy (May 1, 2014-October 16, 2017); and INSTI-containing ART recommended by the DHHS Panel as the single preferred option for initial therapy (October 17, 2017-April 30, 2019). To examine whether racial and ethnic differences varied by sex, analyses were further stratified by sex assigned at birth. Secondary analyses stratified by cohort, patient insurance type, geographic region of residence, and residence in a state that adopted and implemented Medicaid expansion by 2019. Because of the potential for type I error, findings for the stratified analyses should be interpreted as exploratory.

All analyses were performed in SAS 9.4 (SAS Institute) and R 4.0 (R Foundation for Statistical Computing).

Results

Eligible participants included 42 841 US adults newly linked to HIV care at NA-ACCORD sites from October 2007 to April 2019. Of 41 263 adults with information regarding race and ethnicity, 19 378 (47%) identified as Black, 6798 (16%) identified as Hispanic, and 13 539 (33%) identified as White. In comparison with White participants, Black and Hispanic participants were more likely to be female and to be uninsured (**Table**). Eighty-seven percent of Black participants, 88% of Hispanic participants, and 87% of White participants were ever observed to start ART.

Time to Initial ART Prescription by Time Period at Care Entry

Among 33 983 patients linked to care when the DHHS Panel recommended treatment initiation based on CD4+ cell count (October 12, 2007-January 27, 2016), 45.3% of Black patients (95% CI, 44.6% to 46.1%), 50.6% of Hispanic patients (95% CI, 49.3% to 51.9%), and 45.1% of White patients (95% CI, 44.2% to 46.1%) started ART within 1 month of care entry. Compared with White patients, the difference in the probability of ART initiation within 1 month of care entry was 0.2% (95% CI, −1% to 1.4%) for Black patients and 5.4% (95% CI, 3.8% to 7.1%) for Hispanic patients. Among 5128 patients who entered care in the *treat all* era (January 28, 2016-April 30, 2019), 67.6% of Black patients (95% CI, 65.7% to 69.4%), 70.7% of Hispanic patients (95% CI, 67.3% to 74.1%), and 65.6% of White patients (95% CI, 63.3% to 67.9%) started ART within 1 month. Compared with White patients, the difference in the probability of ART initiation within 1 month of care entry was 2% (95% CI, −1% to 4.9%) for Black patients and 5.1% (95% CI, 1% to 9.2%) for Hispanic patients. The probability of ART prescription was significantly higher among Hispanic male patients vs White male

Table. Demographic Characteristics of 42 841 US Adults Entering HIV Care in NA-ACCORD, 2007-2019

Characteristic[a]	No. (%)						
	Non-Hispanic Asian (n = 885)[b]	Non-Hispanic Black (n = 19 378)[b]	Hispanic (n = 6798)[b]	Non-Hispanic Indigenous (n = 174)[b]	Non-Hispanic White (n = 13 539)[b]	Other (n = 489)[c]	Missing (n = 1578)
Year at care entry							
2007-2009	209 (24)	6013 (31)	2040 (30)	38 (22)	4052 (30)	107 (22)	582 (37)
2010-2012	246 (28)	6248 (32)	2414 (36)	60 (35)	4295 (32)	159 (33)	529 (34)
2013-2015	257 (29)	4740 (25)	1641 (24)	54 (31)	3518 (26)	145 (30)	276 (17)
2016-2019	173 (20)	2377 (12)	703 (10)	22 (13)	1674 (12)	78 (16)	191 (12)
Age, y							
18-24	101 (11)	2442 (13)	699 (10)	12 (7)	914 (7)	78 (16)	106 (7)
25-34	331 (37)	4719 (24)	2127 (31)	52 (30)	3005 (22)	158 (32)	288 (18)
35-44	243 (27)	3978 (21)	1748 (26)	42 (24)	3049 (23)	123 (25)	302 (19)
45-54	139 (16)	4780 (25)	1450 (21)	39 (22)	3567 (26)	87 (18)	444 (28)
55-64	57 (6)	2662 (14)	578 (9)	23 (13)	2283 (17)	35 (7)	300 (19)
≥65	14 (2)	797 (4)	196 (3)	6 (3)	721 (5)	8 (2)	138 (9)
Sex							
Female	85 (10)	4141 (21)	886 (13)	16 (9)	1052 (8)	88 (18)	179 (11)
Male	800 (90)	15 237 (79)	5912 (87)	158 (91)	12 487 (92)	401 (82)	1399 (89)
Gender identity	717	12 877	3331	141	10 833	327	1494
Cisgender	708 (98.7)	12 789 (99.3)	3294 (98.9)	137 (97.2)	10 797 (99.7)	323 (98.8)	1491 (99.8)
Transgender	9 (1.3)	88 (0.7)	37 (1.1)	4 (2.8)	36 (0.3)	4 (1.2)	3 (0.2)
Insurance coverage	823	18 051	6438	168	12 557	449	1541
Public	297 (36)	9938 (55)	3173 (49)	120 (71)	7154 (57)	172 (38)	990 (64)
Private	430 (52)	4295 (24)	1468 (23)	30 (18)	3577 (28)	204 (45)	514 (33)
None	96 (12)	3818 (21)	1797 (28)	18 (11)	1826 (15)	73 (16)	37 (2)
Geographic region[d]	856	17 342	6151	164	12 415	458	1435
Northeast/Mid-Atlantic	192 (22)	7446 (43)	2352 (38)	20 (12)	3653 (29)	218 (48)	710 (49)
South	115 (13)	6723 (39)	1838 (30)	45 (27)	4480 (36)	43 (9)	374 (26)
West/North Central	531 (62)	2137 (12)	1887 (31)	87 (53)	3419 (28)	186 (41)	255 (18)
Midwest	18 (2)	1036 (6)	74 (1)	12 (7)	863 (7)	11 (2)	96 (7)
Residence in Medicaid expansion state[e]	(n = 867)	(n = 17 796)	(n = 6201)	(n = 166)	(n = 12 705)	(n = 479)[c]	(n = 1449)
Yes	733 (85)	10 282 (58)	4283 (69)	112 (67)	7612 (60)	425 (89)	1031 (71)
No	134 (15)	7514 (42)	1918 (31)	54 (33)	5093 (40)	54 (11)	418 (29)
County racial and ethnic composition, mean % (SD)							
Non-Hispanic Asian	18 (12)	8 (7)	12 (9)	10 (9)	9 (9)	13 (9)	8 (7)
Non-Hispanic Black	11 (10)	24 (16)	14 (10)	11 (9)	16 (12)	16 (14)	23 (18)
Hispanic	22 (11)	20 (13)	28 (13)	22 (14)	19 (13)	25 (14)	19 (15)
Non-Hispanic Indigenous	0 (1)[f]	0 (1)[f]	0	3 (8)	0 (1)[f]	0	0 (1)[f]
Non-Hispanic White	45 (14)	46 (16)	43 (14)	51 (15)	53 (17)	43 (17)	47 (19)
Other	3 (2)	2 (1)	2 (1)	3 (1)	2 (1)	3 (1)	2 (1)

Abbrevation: NA-ACCORD, North American AIDS Cohort Collaboration on Research and Design.

[a] Demographic data were collected as part of routine clinical care.

[b] Race and ethnicity were self-reported, with response options differing by study site; responses were harmonized across study sites by NA-ACCORD as described in the eAppendix in Supplement 1. Hispanic participants may be of any race; all other groups were non-Hispanic.

[c] Includes participants self-identifying as *other* and those identifying as multiracial and not Hispanic.

[d] Geographic region and county racial and ethnic composition were derived from patient zip code at care entry as described by Edwards et al.[1]

[e] Classified based on whether states had adopted and implemented Medicaid expansion by 2019.

[f] Due to the very low percentage of Indigenous people in most of the counties inhabited by participants, these means are not actually 0, but round down to 0. Standard deviations are greater than the means because a few participants live in counties with a much higher percentage of Indigenous residents (≤55%).

patients (difference, 5.3% [95% CI, 1% to 9.6%]), but was not significantly different among Hispanic female patients vs White female patients (difference, 2.4% [95% CI, −11.4% to 16.2%]) (**Figure 1**, **Figure 2**, and eFigure 3 in Supplement 1).

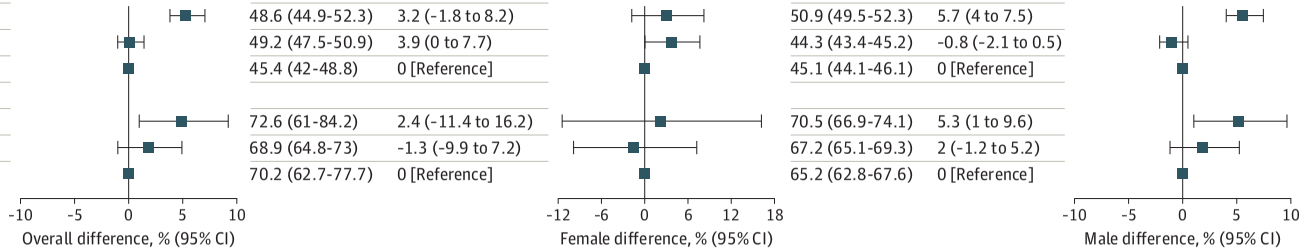
Probability of Being Prescribed INSTI-Containing ART by Time Period at Treatment Initiation

Among patients starting ART, the probability of being prescribed INSTI-containing ART increased from 2007-2019.

Figure 1. Percent of Patients Prescribed ART Within 1 Month of Care Entry and Percent Prescribed an INSTI-Containing Initial ART Regimen by Sex at Birth, Time Period, Race, and Ethnicity, 2007-2019

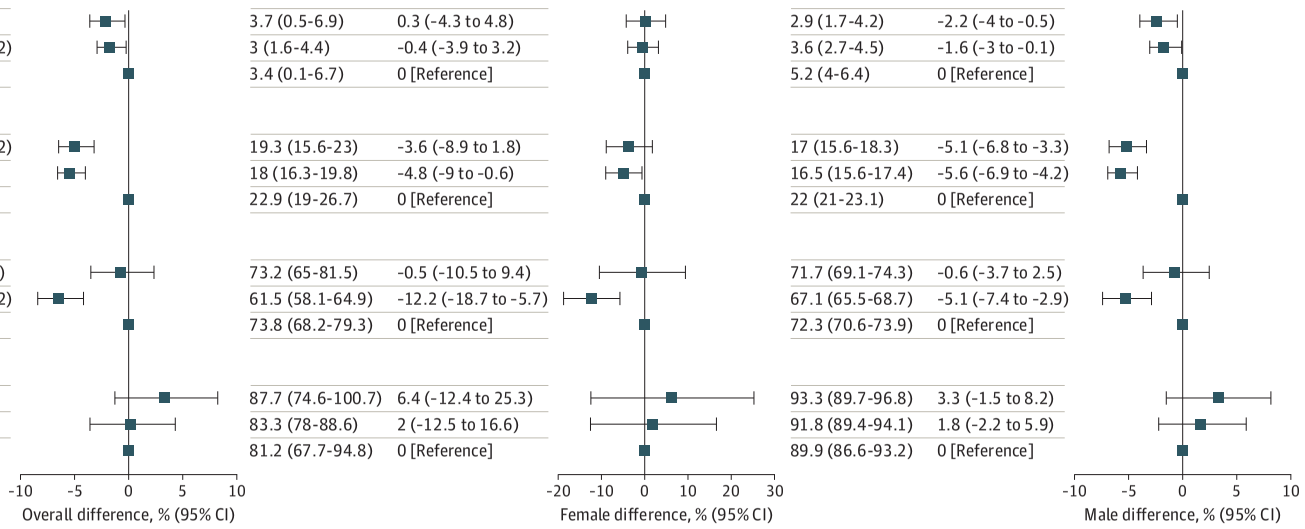
A Started ART at an NA-ACCORD site within 1 month of entering care in NA-ACCORD

Time period at care entry	Overall		Female		Male	
	Percent (95% CI)	Difference, % (95% CI)	Percent (95% CI)	Difference, % (95% CI)	Percent (95% CI)	Difference, % (95% CI)
CD4+-guided treatment initiation (October 12, 2007-January 27, 2016)[a]						
Hispanic	50.6 (49.3-51.9)	5.4 (3.8 to 7.1)	48.6 (44.9-52.3)	3.2 (-1.8 to 8.2)	50.9 (49.5-52.3)	5.7 (4 to 7.5)
Non-Hispanic Black	45.3 (44.6-46.1)	0.2 (-1 to 1.4)	49.2 (47.5-50.9)	3.9 (0 to 7.7)	44.3 (43.4-45.2)	-0.8 (-2.1 to 0.5)
Non-Hispanic White	45.1 (44.2-46.1)	0 [Reference]	45.4 (42-48.8)	0 [Reference]	45.1 (44.1-46.1)	0 [Reference]
Treat all (January 28, 2016-April 30, 2019)[b]						
Hispanic	70.7 (67.3-74.1)	5.1 (1 to 9.2)	72.6 (61-84.2)	2.4 (-11.4 to 16.2)	70.5 (66.9-74.1)	5.3 (1 to 9.6)
Non-Hispanic Black	67.6 (65.7-69.4)	2 (-1 to 4.9)	68.9 (64.8-73)	-1.3 (-9.9 to 7.2)	67.2 (65.1-69.3)	2 (-1.2 to 5.2)
Non-Hispanic White	65.6 (63.3-67.9)	0 [Reference]	70.2 (62.7-77.7)	0 [Reference]	65.2 (62.8-67.6)	0 [Reference]



B Prescribed an INSTI-containing initial ART regimen of those starting ART

Time period at ART initiation	Overall		Female		Male	
	Percent (95% CI)	Difference, % (95% CI)	Percent (95% CI)	Difference, % (95% CI)	Percent (95% CI)	Difference, % (95% CI)
INSTIs approved as salvage therapy (October 12, 2007-July 7, 2009)						
Hispanic	3.1 (1.9-4.2)	-2 (-3.6 to -0.3)	3.7 (0.5-6.9)	0.3 (-4.3 to 4.8)	2.9 (1.7-4.2)	-2.2 (-4 to -0.5)
Non-Hispanic Black	3.5 (2.7-4.2)	-1.6 (-2.9 to -0.2)	3 (1.6-4.4)	-0.4 (-3.9 to 3.2)	3.6 (2.7-4.5)	-1.6 (-3 to -0.1)
Non-Hispanic White	5 (3.9-6.1)	0 [Reference]	3.4 (0.1-6.7)	0 [Reference]	5.2 (4-6.4)	0 [Reference]
INSTIs approved as initial therapy (July 8, 2009-April 30, 2014)						
Hispanic	17.3 (16-18.6)	-4.8 (-6.5 to -3.2)	19.3 (15.6-23)	-3.6 (-8.9 to 1.8)	17 (15.6-18.3)	-5.1 (-6.8 to -3.3)
Non-Hispanic Black	16.8 (16-17.6)	-5.3 (-6.6 to -4)	18 (16.3-19.8)	-4.8 (-9 to -0.6)	16.5 (15.6-17.4)	-5.6 (-6.9 to -4.2)
Non-Hispanic White	22.1 (21.1-23.1)	0 [Reference]	22.9 (19-26.7)	0 [Reference]	22 (21-23.1)	0 [Reference]
INSTIs recommended as an option for initial therapy (May 1, 2014-October 16, 2017)[c]						
Hispanic	71.8 (69.3-74.3)	-0.6 (-3.5 to 2.3)	73.2 (65-81.5)	-0.5 (-10.5 to 9.4)	71.7 (69.1-74.3)	-0.6 (-3.7 to 2.5)
Non-Hispanic Black	66.1 (64.6-67.5)	-6.3 (-8.4 to -4.2)	61.5 (58.1-64.9)	-12.2 (-18.7 to -5.7)	67.1 (65.5-68.7)	-5.1 (-7.4 to -2.9)
Non-Hispanic White	72.4 (70.8-73.9)	0 [Reference]	73.8 (68.2-79.3)	0 [Reference]	72.3 (70.6-73.9)	0 [Reference]
INSTIs recommended as initial therapy for most people with HIV (October 17, 2017-April 30, 2019)[d]						
Hispanic	92.6 (89.2-96.1)	3.5 (-1.3 to 8.2)	87.7 (74.6-100.7)	6.4 (-12.4 to 25.3)	93.3 (89.7-96.8)	3.3 (-1.5 to 8.2)
Non-Hispanic Black	89.5 (87.3-91.8)	0.4 (-3.6 to 4.3)	83.3 (78-88.6)	2 (-12.5 to 16.6)	91.8 (89.4-94.1)	1.8 (-2.2 to 5.9)
Non-Hispanic White	89.2 (85.9-92.4)	0 [Reference]	81.2 (67.7-94.8)	0 [Reference]	89.9 (86.6-93.2)	0 [Reference]



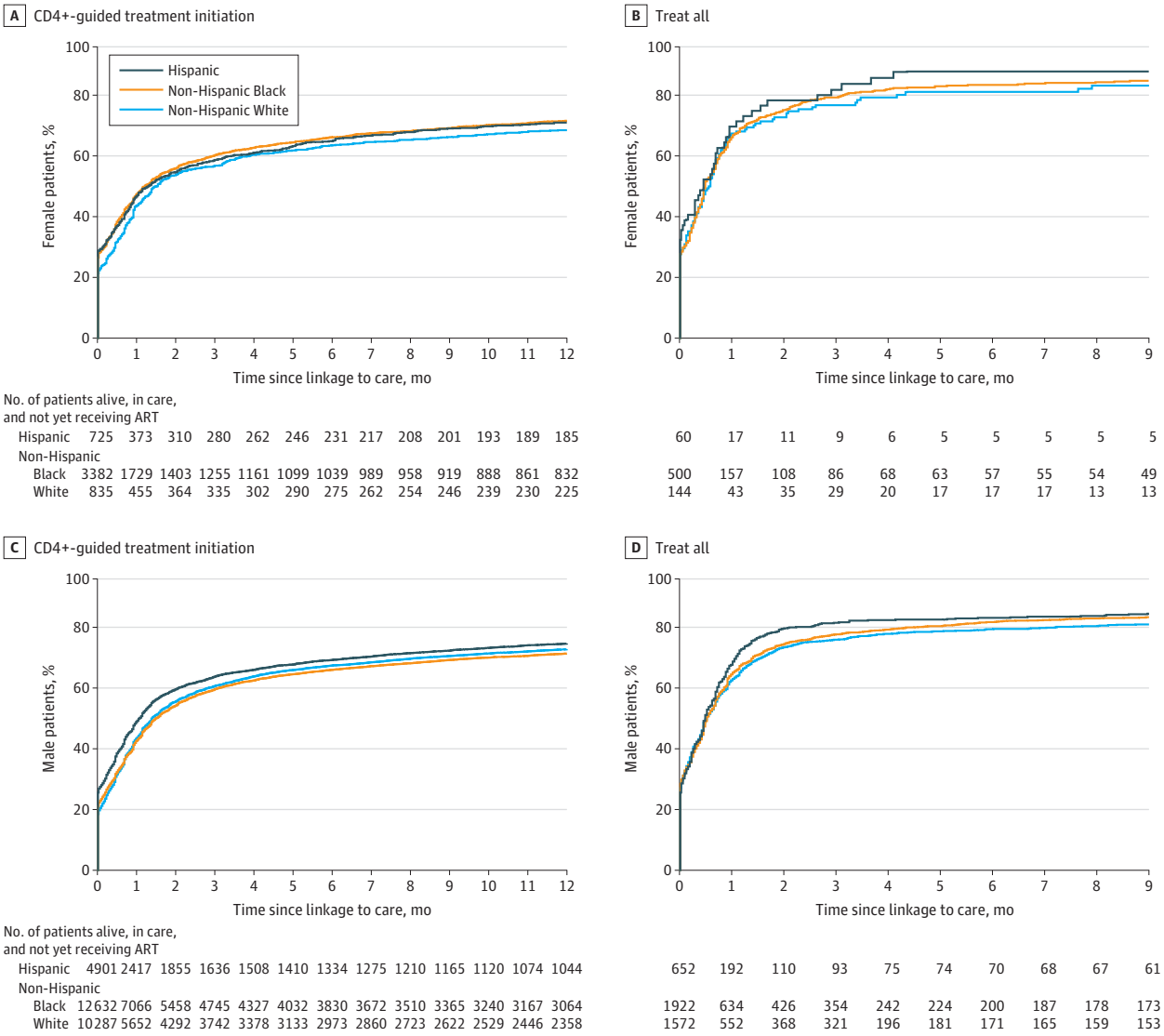
[a] Before 2016, the DHHS Panel recommended that physicians consider patient CD4+ cell count when determining whether to prescribe antiretroviral therapy (ART). The recommended threshold increased from 350 to 500/μL.

[b] On January 28, 2016, based on the results of 2 large randomized clinical trials (START and TEMPRANO), the DHHS Panel strongly recommended treating all HIV-infected patients regardless of CD4+ cell count.

[c] On May 1, 2014, the DHHS Panel recommended a variety of possible regimens for patients initiating ART.

[d] On October 17, 2017, the DHHS Panel recommended INSTI-based regimens as initial therapy for most people with HIV. Boosted PI-based regimens remained recommended only in certain clinical situations, such as when adherence is a concern and resistance testing is not available.

Figure 2. Time to ART Prescription by Treatment Era[a], Sex at Birth, Race, and Ethnicity, 2007-2019[b]



[a] Before 2016, the Department of Health and Human Services (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents recommended that physicians consider patient CD4+ cell count when determining whether to prescribe ART. The recommended threshold for antiretroviral therapy (ART) initiation gradually increased from 350 to 500 cells/μL. On January 28, 2016, the DHHS Panel recommended treating all HIV-infected patients regardless of CD4+ cell count.

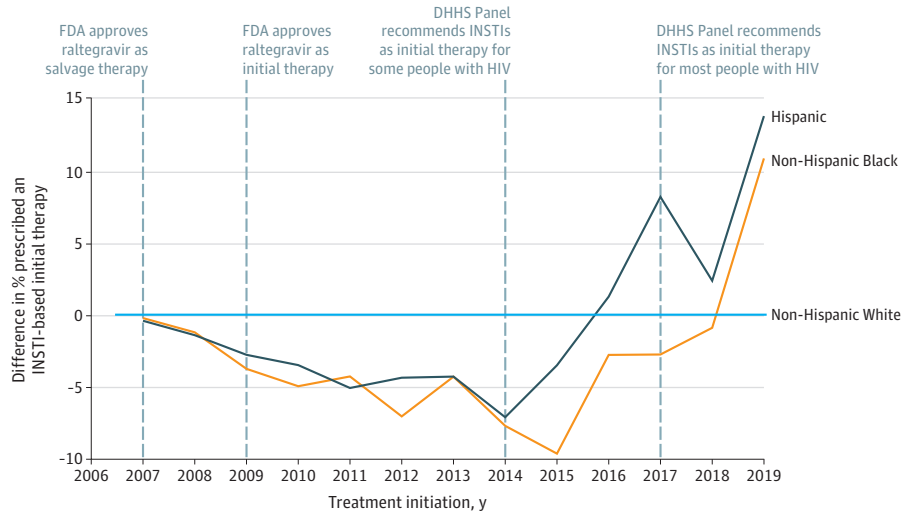
[b] Ns are averaged across imputed data sets.

Curves are truncated at 9 months in the *treat all* era due to small cell sizes.

In 2008, the first full year after the FDA approved raltegravir (the first available INSTI) for treatment-experienced patients, 3% of patients were prescribed INSTI-containing initial ART. By 2018, the first full year after INSTI-containing ART was recommended as the single preferred initial therapy for most people with HIV, 89.9% of Black patients (95% CI, 87.5% to 92.3%), 93.2% of Hispanic patients (95% CI, 89.4% to 96.9%), and 90.8% of White patients (95% CI, 87.4% to 94.2%) starting ART were prescribed an INSTI.

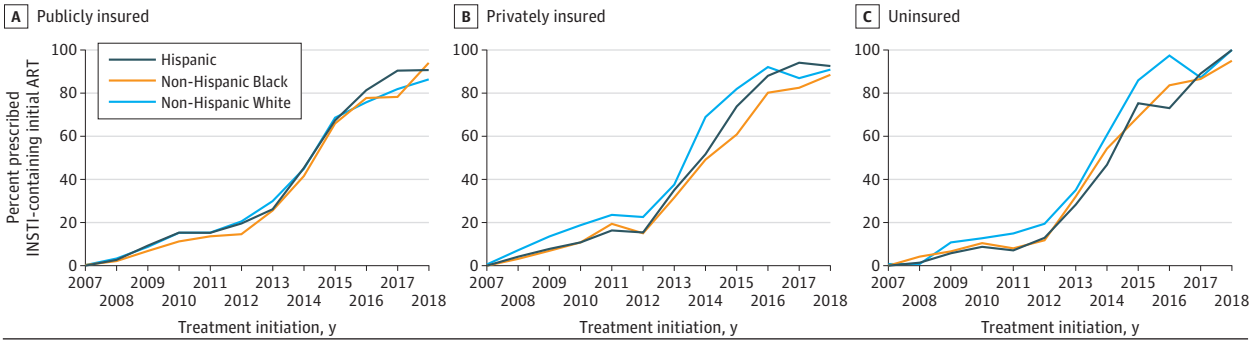
While there were no significant racial or ethnic differences in INSTI prescription among patients starting ART in 2018 or 2019, significant differences were observed in earlier periods (**Figure 3**; eTable 2 and eFigure 4 in Supplement 1). From October 12, 2007 to July 7, 2009, when INSTIs were FDA approved as salvage therapy, 5.0% of White patients, 3.5% of Black patients (difference, −1.6% [95% CI, −2.9% to −0.2%]), and 3.1% of Hispanic patients (difference, −2% [95% CI, −3.6% to −0.3%]) were prescribed INSTIs (Figure 1). From July 8, 2009 to April 30, 2014, when INSTIs were FDA-approved as initial therapy but not yet guideline recommended, 22.1% of White patients, 3.5% of Black patients (difference, −1.6% [95% CI, −2.9% to −0.2%]), and 17.3% of Hispanic patients (difference, −4.8% [95% CI, −6.5% to −3.2%]) were prescribed INSTIs. From May 1, 2014 to October 16, 2017, when the DHHS Panel recommended INSTI-containing ART as an option for initial therapy, there was no

Figure 3. Difference in Percent of Black and Hispanic Patients Relative to White Patients Prescribed an INSTI-Containing Initial ART Regimen by Year at Treatment Initiation, 2007-2019



INSTI indicates integrase strand transfer inhibitor; ART, antiretroviral therapy; FDA, Food and Drug Administration; DHHS Panel, Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents.

Figure 4. Percent of Patients Prescribed an INSTI-Containing Initial ART Regimen by Year at Treatment Initiation, Race, Ethnicity, and Insurance Type, 2007-2018



Data for 2019 not shown due to small cell sizes (Ns <15). INSTI indicates integrase strand transfer inhibitor; ART, antiretroviral therapy.

significant difference in the probability of being prescribed INSTIs between Hispanic patients (71.8%) and White patients (72.4%), but Black patients (66.1%) were still significantly less likely than White patients to be prescribed INSTIs (difference, −6.3% [95% CI, −8.4% to −4.2%]).

Racial and ethnic differences in the prescription of INSTI-containing initial ART were similar by sex except from May 1, 2014 to October 16, 2017, when other regimens were gradually being removed from the DHHS Panel's list of recommended first-line regimens in favor of INSTIs. During that period, while INSTI prescriptions were 5.1% less common (95% CI, −7.4% to −2.9%) among Black male patients compared with White male patients starting ART, they were 12.2% less common (95% CI, −18.7% to −5.7%) among Black female patients compared with White female patients starting ART. During the same period, the probability of INSTI prescription was not significantly different among Hispanic female patients compared with White female patients (Figure 1).

Variation in Racial and Ethnic Differences in INSTI Prescription

Exploratory analyses of factors that may contribute to the observed differences by race and ethnicity suggested that the magnitude of the observed differences may be modified by cohort, geographic region, and residence in a state that had expanded Medicaid, although the observed differences followed a similar pattern across most levels of each of these contextual factors (eTable 2 and eFigures 5, 6, 7, 8, 9, 10, 11, 12, and 13 in Supplement 1). Larger racial and ethnic differences were observed among patients with private health insurance and among uninsured patients than among patients with public health insurance (**Figure 4**; eTables 3 and 4, eFigures 8 and 9 in Supplement 1). The differences were most pronounced from 2014-2016, when INSTIs were recommended as an option for initial therapy but were not yet the preferred initial treatment regimen for most people living with HIV. For example, in 2014, 68.9% of privately insured White patients,

49.2% of privately insured Black patients (difference, −19.8% [95% CI −26.8% to −12.7%]), and 51.7% of privately insured Hispanic patients (difference, −17.2% [95% CI, −26.9% to −7.6%]) were prescribed INSTI-containing initial ART. During the same year, 44.9% of publicly insured White patients, 41.5% of publicly insured Black patients (difference, −3.4% [95% CI, −8.4% to 1.7%]), and 45.3% of publicly insured Hispanic patients (difference, 0.4% [95% CI, −6.5% to 7.3%]) were prescribed INSTI-containing initial ART.

Discussion

Among individuals entering HIV care within a large research consortium in the US from 2007-2019, the 1-month probability of ART prescription was not significantly different across most race and ethnicity comparisons. However, Black and Hispanic individuals were significantly less likely than White individuals to be prescribed INSTI-containing ART for several years after the initial FDA approval of INSTIs but not after national guidelines recommended INSTIs as the single preferred initial treatment regimen for most people with HIV.

Prior studies of INSTI prescribing practices have highlighted prescribing differences among transgender individuals and among persons who are homeless compared with cisgender and stably housed individuals, but these studies were cross-sectional and limited to patient populations in Baltimore, Washington, DC, and San Francisco.[21,22] This study is the first, to our knowledge, to document prescribing differences by race and ethnicity and to examine changes in INSTI prescribing over time in a much larger cohort of patients entering HIV care in the US. While the probability of INSTI prescription was not found to differ significantly among racial and ethnic groups from 2018-2019, differences were observed in earlier years. Furthermore, reductions in disparities corresponded with changes in the guidelines released by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents.

The finding of persistent racial and ethnic disparities in INSTI prescription from 2007-2014, when INSTIs were FDA-approved but not yet standard of care for people initiating ART, is consistent with disparities in the initial rollout of combination ART. Black and Hispanic patients remained less likely to receive combination ART for many years after it became available in the mid-1990s[10,23]—so much so that racial disparities in HIV mortality widened in the late 1990s and 2000s.[24] Previous studies have documented racial and ethnic disparities in ART prescription that could not be explained by differences in patient sex, age, socioeconomic status, insurance coverage, disease severity, or engagement in care.[8-10,25,26] Such disparities are perhaps better explained by the inverse equity hypothesis, which posits that emerging medical treatments often exacerbate health inequities because groups with more power and privilege are better positioned to take advantage of them.[27] This phenomenon has been observed across a broad range of treatments and health outcomes, including statin therapy for high cholesterol,[28] advances in cancer detection and treatment,[29] and recently, vaccines and monoclonal antibody treatments for COVID-19.[30,31] It is also consistent with work linking racism to health disparities through the differential distribution of health-enhancing resources, including money, power, formal education, and beneficial social connections.[32]

While this study did not aim to explain prescribing disparities, exploratory analyses identified possible modification of disparities by patient insurance type, cohort, geographic region, and residence in a state that has expanded Medicaid. In particular, larger disparities were observed among privately insured and uninsured patients than among publicly insured patients, especially from 2014-2016 when INSTIs were recommended as an option for initial therapy but were not yet the preferred initial treatment regimen for most people with HIV. The disparities observed among privately insured and uninsured patients reflect accelerated access to INSTIs among White patients relative to Black and Hispanic patients from 2014-2016. Because White patients tend to have more money, time, and social capital than Black or Hispanic patients,[33] they may have been better equipped to overcome administrative barriers to INSTI prescription, such as preauthorization that was in place before INSTI-containing ART was standard of care. Because the public insurance system is less flexible, it may be less susceptible to differences in access among social groups with different levels of personal resources. This explanation is consistent with previous studies documenting greater disparities in diseases that are more amenable to treatment, and thus whose outcomes are more closely linked to the social and economic resources of individual patients.[29]

Other potential mechanisms not explored in this study include racial bias,[34] differential participation in clinical trials of experimental treatments,[35] differential access to highly specialized physicians,[36] and differential access to new medications through insurance plans.[22,37] For multiply marginalized populations, several factors may interact to compound disparities. For example, women and transgender people with HIV, who have been reported to be more likely to experience weight gain when taking INSTIs, are disproportionately Black and Hispanic.[38] Physicians may be especially reluctant to prescribe INSTIs to Black and Hispanic women due to their disproportionate risk of obesity and cardiometabolic disease, which is itself a consequence of structural racism.[39]

Ensuring equitable access to effective and well-tolerated first-line HIV therapies could help to reduce disparities in treatment continuation and ultimately in long-term survival among people with HIV.[13] The finding that racial and ethnic disparities in the prescription of INSTIs were smaller or no longer evident after national treatment guidelines recommended INSTIs as initial therapy suggests that comprehensive and efficiently updated guidelines may play a role in reducing health disparities among people with HIV. Additional work is needed to understand specific underlying mechanisms, which may include improved coverage by insurance formularies and increased clinician awareness, among other factors.

Limitations

This study has several limitations. First, while study participants were demographically similar to the broader population of US people with HIV, patients receiving care at academic medical centers are overrepresented in NA-ACCORD, so the study findings may not be generalizable to all individuals receiving HIV care in the US.

Second, the results may not reflect the current state of ART prescribing in 2023.

Third, the study population was limited to patients successfully linked to HIV care; given well-documented disparities in HIV diagnosis and linkage to care,[12] prescribing disparities were almost certainly greater when considering the broader population of US adults with HIV.

Fourth, loss to follow-up was treated as a competing risk to avoid overestimating ART initiation among patients lost to follow-up, but some proportion of patients lost to follow-up likely re-entered care or transferred to other clinics where they were prescribed ART. Thus, estimates of the probability of ART initiation are conservative; future work may illuminate disparities in care re-entry and outcomes among patients lost to NA-ACCORD.

Fifth, race and ethnicity may have been misclassified in patient medical records or during the process of imputing missing data on race and ethnicity.

Sixth, because the aim of this study was not to identify discrimination in prescribing practices, the extent to which racial and ethnic differences in time to treatment initiation would have been considered clinically appropriate in the past (ie, prior to the *treat all* era) was not assessed. Due to persistent inequities in access to care and treatment, Black and Hispanic patients tend to receive treatment later (ie, at lower CD4+ cell counts) than White patients[13]; consequently, disparities in timely treatment initiation among patients clinically eligible to start treatment may be greater than the disparities described in this study.

Conclusions

Among adults entering HIV care within a large US research consortium from 2007-2019, the 1-month probability of ART prescription was not significantly different across most races and ethnicities, although Black and Hispanic patients were significantly less likely than White patients to receive INSTI-containing ART in earlier time periods but not after INSTIs became guideline-recommended initial therapy for most people with HIV. Additional research is needed to understand the underlying racial and ethnic differences and whether the differences were associated with clinical outcomes.

ARTICLE INFORMATION

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Author Affiliations: Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill (Zalla, Cole, Adimora, Vines, Edwards); Now with Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Zalla); Division of Infectious Diseases, School of Medicine, University of North Carolina at Chapel Hill (Eron, Adimora); Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Althoff, Coburn, Lang, Gebo); Kaiser Permanente Northern California, Oakland (Silverberg); Mid-Atlantic Permanente Research Institute, Kaiser Permanente Mid-Atlantic States, Rockville, Maryland (Horberg); Division of Infectious Diseases, School of Medicine, Emory University, Atlanta, Georgia (Marconi); Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia (Marconi); Department of Health Systems and Population Health, School of Public Health, University of Washington, Seattle (Williams); Center of Innovation for Veteran-Centered and Value-Driven Care, US Department of Veterans Affairs, Seattle, Washington (Williams); Department of Medicine, University of Calgary, Calgary, Alberta, Canada (Gill); Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland (Gebo, Moore); Division of Infectious Diseases and Chronic Viral Illness Service, McGill University, Montreal, Quebec, Canada (Klein); Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee (Sterling); Division of Epidemiology, School of Medicine, Vanderbilt University, Nashville, Tennessee (Rebeiro); Division of Infectious Diseases, School of Medicine, Vanderbilt University, Nashville, Tennessee (Rebeiro); Clinical Research Center, Universidad Central del Caribe, Bayamón, Puerto Rico (Mayor).

Author Contributions: Dr Zalla had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Zalla, Cole, Eron, Lang, Klein, Rebeiro, Mayor, Edwards.
Acquisition, analysis, or interpretation of data: Zalla, Cole, Eron, Adimora, Vines, Althoff, Silverberg, Horberg, Marconi, Coburn, Williams, Gill, Gebo, Sterling, Rebeiro, Moore, Edwards.
Drafting of the manuscript: Zalla, Althoff, Coburn, Williams, Gill, Mayor, Edwards.
Critical revision of the manuscript for important intellectual content: Zalla, Cole, Eron, Adimora, Vines, Silverberg, Horberg, Marconi, Coburn, Lang, Williams, Gill, Gebo, Klein, Sterling, Rebeiro, Mayor, Moore, Edwards.
Statistical analysis: Zalla, Cole, Edwards.
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