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MAJOR ARTICLE

Integrase Inhibitor Prescribing Disparities in the DC and Johns Hopkins HIV Cohorts

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Integrase inhibitors (INSTIs) are recommended by expert panels as initial therapy for people with HIV. Because there can be disparities in prescribing and uptake of novel and/or recommended therapies, this analysis assessed potential INSTI prescribing disparities using a combined data set from the Johns Hopkins HIV Clinical Cohort and the DC Cohort. We performed multivariable logistic regression to identify factors associated with ever being prescribed an INSTI. Disparities were noted, including clinic location, age, and being transgender. Identifying disparities may allow clinicians to focus their attention on these individuals and ensure that therapy decisions are grounded in valid clinical reasons.

Keywords. cohort; disparities; HIV; integrase strand transfer inhibitors (INSTIs); transgender.

US Department of Health and Human Services (DHHS) guidelines for first-line antiretroviral therapy (ART) are regularly updated. Currently, the guidelines only recommend integrase strand transfer inhibitors (INSTIs) for initial ART for most patients [1]. INSTIs are efficacious in ART-naïve [2–4] and ART-experienced patients [3, 5] and generally well tolerated, with a high barrier to resistance [6]. Greater regimen persistence with INSTI-based compared with non-INSTI-based regimens has been demonstrated [7]. However, there have been concerns regarding adverse metabolic effects, including weight gain [8, 9], and neural tube defects with in utero INSTI exposure [10].

Many factors potentially influence INSTI prescribing: patient or provider preference, insurance and copays, comorbidities, childbearing potential and/or pregnancy, tolerability, and ART resistance [11]. It is unknown what effects, if any, the DHHS guidelines for INSTI use in treatment-naïve patients have had on INSTI prescription in treatment-experienced patients. It is possible that providers might extrapolate the recommendation that ART-naïve patients use an INSTI for ART-experienced patients, including recommending a change to INSTI for patients who are tolerating a non-INSTI regimen and are virally suppressed. Whether that change would be recommended and/or accepted uniformly across all demographic groups is unknown. Prescribing disparities have been observed for other medical conditions [12, 13]. If disparities exist, they may be detrimental in terms of overall HIV outcomes because INSTIs are favored due to their potency and tolerability. Our objective was to describe INSTI prescribing prevalence and examine disparities in INSTI prescribing in 2 different locations in the Mid-Atlantic States area.

METHODS

This secondary data analysis used DC Cohort and Johns Hopkins HIV Clinical Cohort (JHHCC) data.

Since 2011, the DC Cohort has enrolled participants receiving care at 15 HIV clinics in Washington, DC. Participants' sociodemographic, HIV/AIDS-related, encounter, diagnosis, treatment (antiretroviral therapy and others), and laboratory test information is collected from electronic health records (EHRs) supplemented with manual abstraction [14, 15]. The JHHCC is an observational cohort of individuals receiving HIV care at the John G. Bartlett Specialty Practice at Johns Hopkins Medicine (Baltimore, MD, USA), which started in 1989. Laboratory, diagnostic, clinical, pharmaceutical, behavioral, and social data are collected at enrollment. Subsequent information is collected over time through medical records, the Johns Hopkins Health System databases, medical records from other facilities, vital records, and automated computer-assisted self-interviews [16].

Patient Consent

The DC Cohort is approved by the Institutional Review Board at the George Washington University, and all participants sign

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written informed consent. The Johns Hopkins HIV Clinical Cohort is approved by the Institutional Review Board at the Johns Hopkins University, and all participants sign written informed consent.

Inclusion Criteria

Included participants were ≥18 years old, had at least 1 encounter between 4/1/17 and 3/31/19, and had been prescribed ART before their last encounter.

Outcome of Interest

All variables for this analysis were defined using an index visit of each participant's last encounter between 4/1/17 and 3/31/19. Prescription data from the EHRs were used to determine INSTI prescription status: current, previous, or never prescribed an INSTI. "Ever prescribed an INSTI" was comprised of participants with current and prior INSTI prescription. Additional characteristics of the current regimen were determined, that is, whether the patient was additionally prescribed a protease inhibitor or non-nucleoside reverse transcriptase inhibitor (NNRTI). Nucleoside reverse transcriptase inhibitors (NRTIs) serving as backbone agents were not examined in this analysis.

Additional Covariates

Variable determination differed slightly between DC Cohort and JHHCC (Supplemental Table 1). Demographic covariates included age, gender, and sexual risk behavior, race/ethnicity, insurance status, and time since first HIV care visit at the clinic. HIV-related covariates included presence/absence of drug resistance mutations (IAS 2019 update [17]) and CD4 (last recorded and nadir) and last recorded HIV RNA values. Additional clinical covariates included history of intravenous drug use, current alcohol or tobacco use, and presence of chronic hepatitis B, chronic hepatitis C, and metabolic comorbidities (chronic kidney disease [CKD], diabetes mellitus [DM]).

Statistical Analysis

We compared the demographic and clinical characteristics of individuals by INSTI prescription status using descriptive statistics, including frequencies and percentages for categorical variables and medians and interquartile ranges for continuous variables.

Adjusted multivariable logistic regression (Table 2) was used to evaluate associations of demographic and clinical factors with the outcome ($P < .05$ considered statistically significant). Analyses were conducted using SAS, version 9.4 (Cary, NC, USA).

RESULTS

Of the 9558 participants, 6839 (71.5%) were currently prescribed an INSTI and 754 (7.9%) were previously prescribed an INSTI, for a total of 79.4% ever prescribed an INSTI. A sizeable minority of 1965 (20.6%) were never prescribed an INSTI. Of those currently prescribed an INSTI, 47.9% were prescribed dolutegravir, 27.7% were prescribed elvitegravir, 16.8% were prescribed bictegravir, and 7.5% were prescribed raltegravir.

The highest proportion of current INSTI prescriptions (81.1%) was in the youngest age group (age 18–24 years), while the lowest (68.2%) was in the 40–49-year-old age group ($P < .0001$ across age groups) (Table 1). Transgender females had the lowest proportion of current prescriptions when comparing by gender (57.6%; $P = .0017$). There were no differences by race. Supplementary Table 2 displays JHHCC/DC Cohort differences. Overall, 87.5% of Johns Hopkins participants had ever been prescribed INSTIs compared with 76.9% of DC Cohort participants. Five DC Cohort sites were comparable to Hopkins, with the proportion prescribed an INSTI ranging from 83.5% to 89.7%, whereas 10 ranged from 66.7% to 79.8%.

Demographic factors associated with having ever been prescribed an INSTI included receiving care at Hopkins (adjusted odds ratio [aOR], 1.97 compared with DC; 95% CI, 1.69–2.29) and being younger (aOR, 2.15 for 18–24-year-olds compared with those aged ≥50 years; 95% CI, 1.42–3.26) (Table 2). Transgender females were less likely to have been prescribed an INSTI (aOR, 0.62; 95% CI, 0.43–0.89). No differences by race or insurance type were observed. Those with longer HIV care duration were less likely to have been prescribed an INSTI (aOR, 0.98 per each 5-year increase; 95% CI, 0.97–0.99). Alcohol abuse was associated with having ever been prescribed an INSTI (aOR, 1.29; 95% CI, 1.12–1.47), as was the presence of NRTI (aOR, 1.85; 95% CI, 1.50–2.27) and NNRTI (aOR, 1.50; 95% CI, 1.25–1.82) drug resistance mutations.

DISCUSSION

In this study of individuals on antiretroviral therapy in the Washington, DC/Baltimore metropolitan area, most participants had been prescribed INSTIs, with close to three-quarters of all participants currently prescribed an INSTI. However, disparities were noted, including location, age, and being transgender. This study uniquely adds to the HIV medical literature by examining INSTI prescription prevalence in a contemporary cohort and demonstrating disparities in the use of INSTI.

Our results are consistent with prior studies that INSTI prescription is common among individuals initiating therapy [18, 19] and changing therapy [20]. Prior work in the Medical Monitoring Project showed that prescription of INSTI increased from 43.4% to 50.7% from 2015–2016 to 2016–2017 [19]; we found 71.6% in 2019.

In our sample, younger individuals were more likely to have been prescribed an INSTI. Younger individuals with newer HIV diagnoses may have started therapy after the DHHS guidelines recommending INSTIs as first-line therapy were released, making them more likely to have started and persisted

Table 1. Demographic and Clinical Characteristics of Participants With Current, Previous, and Never INSTI Use, DC Cohort and Johns Hopkins HIV Clinical Cohort, 2017–2019

	Currently on INSTI	Previously on INSTI	Never on INSTI	
	No. (Row %)	No. (Row %)	No. (Row %)	*P*
Overall (n = 9558)	6839 (71.5)	754 (7.9)	1965 (20.6)	—
Clinic location				<.0001
Baltimore—Hopkins (n = 2302)	1796 (78.0)	219 (9.5)	287 (12.5)	
DC (n = 7256)	5043 (69.5)	535 (7.4)	1678 (23.1)	
Age, y				<.0001
18–24 (n = 206)	167 (81.1)	11 (5.3)	28 (13.6)	
25–39 (n = 1713)	1222 (71.3)	115 (6.7)	376 (21.9)	
40–49 (n = 1860)	1269 (68.2)	151 (8.1)	440 (23.7)	
50+ (n = 5779)	4181 (72.3)	477 (8.3)	1121 (19.4)	
Gender and sexual risk behavior[a]				.0017
Cisgender male—MSM (n = 3376)	2390 (70.8)	269 (8.0)	717 (21.2)	
Cisgender male—heterosexual (n = 3165)	2297 (72.6)	229 (7.2)	639 (20.2)	
Cisgender female (n = 2856)	2059 (72.1)	239 (8.4)	558 (19.5)	
Transgender female (n = 151)	87 (57.6)	16 (10.6)	48 (31.8)	
Transgender male (n = 10)	6 (60)	1 (10)	3 (30)	
Race/ethnicity				.29
Non-Hispanic Black (n = 7386)	5294 (71.7)	589 (8.0)	1503 (20.3)	
Non-Hispanic White (n = 1332)	952 (71.5)	104 (7.8)	276 (20.7)	
Hispanic (n = 514)	377 (73.3)	36 (7.0)	101 (19.7)	
Other/unknown (n = 326)	216 (66.2)	25 (7.7)	85 (26.1)	
Insurance status[a]				<.0001
Public (n = 5956)	4374 (73.4)	428 (7.2)	1154 (19.4)	
Private (n = 3175)	2151 (67.7)	301 (9.5)	723 (22.8)	
No insurance (n = 147)	111 (75.5)	2 (1.4)	34 (23.1)	
Insurance type unknown (n = 280)	203 (72.5)	23 (8.2)	54 (19.3)	
Last recorded HIV viral load, copies/mL				.030
<200	5383 (78.7)	565 (74.9)	1537 (78.2)	
200+	606 (8.9)	92 (12.2)	170 (8.7)	
Unknown	850 (12.4)	97 (12.9)	258 (13.1)	
	Currently on INSTI (n = 6839)	Previously on INSTI (n = 754)	Never on INSTI (n = 1965)	
	No. (Col %)	No. (Col %)	No. (Col %)	*P*
Current alcohol abuse	1614 (23.6)	156 (20.7)	412 (21.0)	.017
Current smoking	2658 (38.9)	263 (34.9)	738 (37.6)	.078
History of injection drug use	970 (14.2)	119 (15.8)	207 (10.5)	<.0001
Years since first HIV care visit at clinic, median (IQR)[b]	9.4 (5.3–14.3)	9.6 (5.6–15.4)	9.4 (6.3–13.3)	.19
HIV drug resistance mutations[a]				
Major NRTI mutation present	1303 (19.1)	156 (20.7)	165 (8.4)	<.0001
Major NNRTI mutation present	1258 (18.4)	124 (16.4)	183 (9.3)	<.0001
Major PI mutation present	569 (8.3)	53 (7.0)	80 (4.1)	<.0001
Major INSTI mutation present	101 (1.5)	28 (3.7)	22 (1.1)	<.0001

Abbreviations: INSTI, integrase strand transfer inhibitor; IQR, interquartile range; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

[a]See Supplementary Table 1 for definitions.

[b]There were 183 missing values for years since first HIV care visit.

on INSTI therapy. We found that individuals who had NRTI and NNRTI drug resistance mutations were more likely to have been prescribed an INSTI. This may represent prior virologic failure necessitating a switch to INSTI. Individuals who were never prescribed an INSTI may be more likely to have more stability in their HIV regimen history overall, possibly having not experienced virologic failure and/or having had a longer duration of HIV.

We also found that being a transgender female was associated with not being prescribed an INSTI. Although INSTIs

Table 2. Adjusted[a] Analysis of Demographic and Clinical Characteristics Associated With Ever Having Been Prescribed an INSTI vs Never Having Been Prescribed an INSTI (n = 9558)[b]

	Ever (n = 7442) vs Never (n = 1933) on an INSTI
	Adjusted OR (95% CI)
Clinic location	
Baltimore—Hopkins	Ref
DC	1.97 (1.69–2.29)*
Age, y	
18–24	2.15 (1.42–3.26)*
25–39	1.05 (0.90–1.22)
40–49	0.92 (0.80–1.06)
50+	Ref
Gender and sexual risk behavior	
Cisgender male—MSM	Ref
Cisgender male—heterosexual	0.94 (0.82–1.07)
Cisgender female	1.02 (0.89–1.18)
Transgender female	0.62 (0.43–0.89)*
Transgender male	0.63 (0.16–2.51)
Race/ethnicity	
Non-Hispanic White	Ref
Hispanic	1.22 (0.93–1.60)
NH Black	0.95 (0.81–1.12)
Other	0.74 (0.49–1.10)
Unknown	0.98 (0.67–1.43)
Insurance status	
Public	Ref
Private	1.02 (0.90–1.15)
Other	0.88 (0.59–1.31)
Unknown	0.92 (0.67–1.27)
Current alcohol abuse	1.29 (1.12–1.47)*
HIV drug resistance mutations	
Major NRTI mutation present (vs absent)	1.85 (1.50–2.27)*
Major NNRTI mutation present (vs absent)	1.50 (1.24–1.82)*
Major PI mutation present (vs absent)	1.25 (0.95–1.63)
Major INSTI mutation present (vs absent)	0.96 (0.60–1.55)
Years since first HIV care visit at clinic (per 5-y increase)[b]	0.98 (0.97–0.99)*

Abbreviations: IDU, injection drug use; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; OR, odds ratio; PI, protease inhibitor.

*$P < .05$.

[a]Analysis adjusted for all factors shown in Table 2 plus the following defined in Supplementary Table 1: chronic hepatitis B, chronic hepatitis C, diabetes, chronic kidney disease, and the following: last recorded and nadir CD4 count, current smoking, history of IDU, and last recorded HIV RNA level.

[b]There were 183 participants in the DC Cohort who had missing values for years since first HIV care visit at the clinic and were excluded from the adjusted analysis.

are considered least likely to interfere with gender-affirming hormone therapy [1], transgender women may be hesitant to use newer ART agents and/or prescribers may be more hesitant to prescribe because of concerns about ART–hormone interactions [21]. Transgender women experience discrimination within the health care system and are less likely to be retained in care and achieve viral suppression, and our findings may reflect less engagement by providers of transgender women [22, 23].

We noted geographic disparities in INSTI prescribing, with more individuals at Hopkins having ever been prescribed an INSTI. This raises the question of how geographic areas influence prescribing patterns. Prior work has not focused specifically on regional patterns of ART prescribing by ART class. However, other ART-related outcomes, like time to ART initiation, have been shown to vary along regional lines [24]. It is unclear what is driving the difference in prescribing between DC and Hopkins. The DC Cohort practices represent a mix of hospital- and community-based clinics. Within DC, there were no unifying characteristics of the lower-prescribing clinics, such as size or hospital- vs community-based practice.

The strengths of our study are that we had a large sample size covering a large metropolitan area. We were able to use our data set to identify differences between people with HIV prescribed and not prescribed INSTIs, illuminating disparities in INSTI

prescribing. Our main limitation is that no detailed information about reasons for stopping/switching therapy were available.

In summary, we found differences by clinic location, age, and gender in INSTI usage. Further research, including both qualitative research and quantitative research incorporating individuals receiving HIV care in additional geographic areas, may provide additional insights.

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