

Sexually Transmitted Infections Among HIV-Infected Individuals in the District of Columbia and Estimated HIV Transmission Risk: Data From the DC Cohort

Jose Lucar,^{1,2,6} Rachel Hart,³ Nabil Rayeed,³ Arpi Terzian,⁴ Amy Weintrob,^{1,2} Marc Siegel,¹ David M. Parenti,¹ Leah E. Squires,^{2,5} Rush Williams,^{2,7} Amanda D. Castel,⁴ and Debra A. Benator^{1,2}, for the DC Cohort Executive Committee

¹Division of Infectious Diseases, The George Washington University Medical Center, Washington, DC; ²Infectious Diseases Section, Veterans Affairs Medical Center, Washington, DC; ³Cerner Corporation, Kansas City, Missouri; ⁴Milken School of Public Health and ⁵Department of Psychology, The George Washington University, Washington, DC; ⁶Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, Mississippi; ⁷Columbia Health, Columbia University in the City of New York, New York, New York

Background. Washington, DC, has one of the highest rates of HIV infection in the United States. Sexual intercourse is the leading mode of HIV transmission, and sexually transmitted infections (STIs) are a risk factor for HIV acquisition and transmission.

Methods. We evaluated the incidence and demographic factors associated with chlamydia, gonorrhea, and syphilis among HIV-infected persons enrolled at 13 DC Cohort sites from 2011 to 2015. Using Poisson regression, we assessed covariates of risk for incident STIs. We also examined HIV viral loads (VLs) at the time of STI diagnosis as a proxy for HIV transmission risk.

Results. Six point seven percent (451/6672) developed an incident STI during a median follow-up of 32.5 months (4% chlamydia, 3% gonorrhea, 2% syphilis); 30% of participants had 2 or more STI episodes. The incidence rate of any STIs was 3.8 cases per 100 person-years (95% confidence interval [CI], 3.5–4.1); age 18–34 years, 10.8 (95% CI, 9.7–12.0); transgender women, 9.9 (95% CI, 6.9–14.0); Hispanics, 9.2 (95% CI, 7.2–11.8); and men who have sex with men (MSM), 7.7 (95% CI, 7.1–8.4). Multivariate Poisson regression showed younger age, Hispanic ethnicity, MSM risk, and higher nadir CD4 counts to be strongly associated with STIs. Among those with an STI, 41.8% had a detectable VL within 1 month of STI diagnosis, and 14.6% had a VL ≥ 1500 copies/mL.

Conclusions. STIs are highly prevalent among HIV-infected persons receiving care in DC. HIV transmission risk is considerable at the time of STI diagnosis. Interventions toward risk reduction, antiretroviral therapy adherence, and HIV virologic suppression are critical at the time of STI evaluation.

Keywords. District of Columbia; HIV; human immunodeficiency virus; sexually transmitted infections; STI.

According to data from the Centers for Disease Control and Prevention, the District of Columbia had one of the highest incidence rates of HIV infection in adults and adolescents living in the United States in 2015, at 66.1 cases per 100 000 population [1]. As of 2015, the prevalence of HIV infection in DC was 2.0%, which exceeded the World Health Organization definition of 1% as a generalized epidemic [2]. The leading mode of HIV transmission for new diagnoses from 2011 to 2015 was sexual contact (76%). Men who have sex with men (MSM) accounted for 58% of those new cases, whereas heterosexually identified men and women accounted for 16%.

Sexually transmitted infections (STIs) are a well known risk factor for HIV acquisition and transmission [3–8]. Both ulcerative and nonulcerative STIs provide a portal of entry for HIV

through mucosal disruption and inflammation, and by increasing HIV RNA in genital secretions. There is a direct correlation between plasma and genital HIV RNA concentrations, which underscores the importance of antiretroviral therapy (ART) to prevent HIV transmission [9]. In the presence of an STI, genital HIV shedding can occur despite being on ART with plasma HIV RNA suppression [10]. On the other hand, a multicenter randomized controlled trial comparing early vs delayed ART initiation in HIV-serodiscordant heterosexual couples showed that early ART was associated with a 93% lower risk of linked-partner infection [11]. Also, a European prospective observational study in HIV-serodiscordant heterosexual and MSM couples having condomless sex showed no linked HIV transmission when the viral load was undetectable on ART [12].

This study aimed to describe the incidence and demographic factors associated with the development of chlamydia, gonorrhea, and syphilis in people living with HIV in care in DC. We also examined plasma HIV viral loads (VLs) at the time of STI diagnosis as an approximation of HIV transmission risk.

METHODS

The DC Cohort is a clinic-based, city-wide, longitudinal observational cohort launched in 2011 to better understand HIV

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 Correspondence: J. Lucar, MD, University of Mississippi Medical Center, 2500 N State St, Suite N502, Jackson, MS 39216 (jlucarloveras@umc.edu).

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epidemiology in DC, describe clinical outcomes among those in care, and improve the quality of care for people living with HIV in the DC metropolitan area [13]. At the time of this analysis, there were 13 participating outpatient sites: 8 hospital-based clinics and 5 community-based clinics. Following the provision of written informed consent, participants' clinical data was manually entered or electronically exported from patient medical records and entered into a web-based data entry system called Discovere (Cerner Corporation, Kansas City, MO). Details of the DC Cohort study design have been described previously [14, 15].

Study Population and Design

Eligible participants included those enrolled from January 1, 2011, to March 31, 2015. Participant follow-up time included time from enrollment to June 30, 2015, or until the first of these occurred: death, withdrawal from the DC Cohort, or loss to follow-up. Demographic and clinical characteristics were collected at study enrollment. A descriptive, retrospective cohort design was used to examine the incidence of confirmed cases of chlamydia, gonorrhea, and syphilis, as well as the VLs in individuals with any STIs, 1 STI, and 2 or more STIs. As STI screening may be unevenly applied between study sites, true incidence is not known. However, incidence here will refer to those cases detected by testing in association with either symptoms or potential exposure, and by clinician- or program-directed screening in asymptomatic participants.

Participants newly diagnosed with chlamydia, gonorrhea, and syphilis more than 30 days after study enrollment were defined as incident STI cases. An incident case of chlamydia or gonorrhea was defined as a positive nucleic acid amplification test (NAAT) or culture on urogenital or extragenital specimens; a subsequent new case was accepted as such if there was a positive test ≥ 3 weeks after the previous positive test. An incident case of syphilis was defined as having (i) positive nontreponemal test (NTr) titer of $\geq 1:8$ with a previous nonreactive NTr, (ii) 4-fold increase in the NTr titer from the previous test, or (iii) positive treponemal test (Tr) if a NTr titer was $\geq 1:8$ and the previous Tr test was negative. A possible incident syphilis case was defined as a single, high-titer NTr test of $\geq 1:32$ that otherwise did not fit the criteria for a true incident case. An STI episode may include any combination of chlamydia, gonorrhea, and syphilis diagnosed at the same date. The occurrence and number of incident STI episodes among participants was assessed.

To evaluate the HIV transmission potential in individuals with incident STIs, we also examined their plasma HIV VLs. We determined the VLs at the time of STI diagnosis, defined as the VL within ± 1 month, 3 months, and 6 months of the STI diagnosis date. If a participant had 2 or more STI episodes within each ± 1 -, 3-, or 6-month period, the highest VL was selected. Subsequently, we categorized the individuals with STIs as either having any number, 1, or 2 or more STIs, as well as their VLs as either < 1500 or ≥ 1500 copies/mL. This cutoff was used given

previous data that HIV-infected persons with VLs higher than 1500 copies/mL had an increased risk of transmitting HIV to others [8, 16]. Because the risk of HIV transmission increases as the plasma viral load increases [8, 17], we performed a second analysis using the following cutoffs: less than the lower limit of quantification ($< \text{LLOQ}$), $\text{LLOQ} - < 1500$, $1500 - < 10\,000$, and $\geq 10\,000$ copies/mL. Of note, more than 99% of the VLs included in this analysis had an LLOQ of either 20 or 40 copies/mL.

Statistical Analysis

Frequencies on demographic and clinical characteristics at study enrollment were measured. Differences by factor across a specific STI (chlamydia, gonorrhea, syphilis) were determined using chi-square test statistics and Fisher exact tests for categorical variables and Wilcoxon rank-sum tests for continuous variables, excluding other and unknown values. Incidence rates were calculated per 100 person-years (P-Y) of observation, using Rothman/Greenland estimation for 95% confidence intervals (CIs). Univariate and multivariate Poisson regression analyses were conducted for factors associated with STIs using a Bonferroni correction (to account for multiple testing), resulting in a significance level of $.05/3 = .0167$, and subsequent confidence intervals were set at 98.33%. Characteristics with unknown values were multiply imputed in the Poisson model. All analyses were conducted in SAS 9.4 (Cary, NC).

Ethics

The George Washington University Institutional Review Board (IRB), the DC-DOH IRB, and the IRBs of the individual study sites approved the study protocol, consent forms, and research instruments.

RESULTS

Around the time this data set was closed, the estimated population of persons with HIV infection receiving care at the 13 DC Cohort sites was 11 235, of which 8732 persons (77.7%) were approached for enrollment. Of those persons approached, 7004 (80.2%) were consented, 948 (10.9%) declined enrollment, 14 (0.2%) withdrew consent, and 766 (8.8%) remained undecided. There were significant differences between those consenting and declining, which included female gender (27.8% of those consenting vs 36.1% of those declining, $P < .0001$), white race/ethnicity (13.1% of those consenting vs 6.6% of those declining, $P < .0001$), and private insurance status (27.6% of those consenting vs 33.2% of those declining, $P < .0001$).

Among the 6762 participants enrolled in the study between January 1, 2011, and March 31, 2015, the median age at consent was 47 years (interquartile range, 36.5–54.5 years); 71% were male, 76% were non-Hispanic black, 39% were MSM, and 29% were heterosexual participants. There were 113 (2%) transgender women and 5 (0.1%) transgender males enrolled in the study (Table 1). At the time of consent, 7.8% of participants were known to be homeless or have unstable housing, 63.8%

Table 1. Baseline Characteristics^a of the DC Cohort Participants by Incident STIs (n = 6762)

	Total		Chlamydia			Gonorrhea			Syphilis			Any STI		
	No.	Column %	No.	Row %	Column %	No.	Row %	Column %	No.	Row %	Column %	No.	Row %	Column %
	6762		250	3.7		212	3.1		123	1.8		451	6.7	
Age at enrollment, y														
0–17	149	2.2	10	6.7	4.0	7	4.7	3.3	1	0.7	0.8	11	7.4	2.4
18–34	1377	20.4	137	9.9	54.8	114	8.3	53.8	45	3.3	36.6	220	16.0	48.8
35–54	3637	53.8	95	2.6	38.0	80	2.2	37.7	69	1.9	56.1	196	5.4	43.5
55+	1599	23.6	8	0.5	3.2	11	0.7	5.2	8	0.5	6.5	24	1.5	5.3
Age at consent, median (IQR)	470 (36.5–54.5)		32.8 (25.6–42.3)			32.1 (26.0–42.9)			38.9 (31.6–47.4)			34.8 (26.9–44.3)		
Gender at consent														
Male	4823	71.3	210	4.4	84.0	187	3.9	88.2	116	2.4	94.3	392	8.1	86.9
Female	1821	26.9	29	1.6	11.6	15	0.8	7.1	3	0.2	2.4	39	2.1	8.6
Transgender female	113	1.7	11	9.7	4.4	10	8.8	4.7	4	3.5	3.3	20	17.7	4.4
Transgender male	5	0.1	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Race/ethnicity ^b														
Non-Hispanic black	5161	76.3	169	3.3	67.6	132	2.6	62.3	75	1.5	61.0	290	5.6	64.3
Non-Hispanic white	940	13.9	54	5.7	21.6	52	5.5	24.5	28	3.0	22.8	101	10.7	22.4
Hispanic	314	4.6	21	6.7	8.4	23	7.3	10.8	11	3.5	8.9	43	13.7	9.5
Other	137	2.0	3	2.2	1.2	4	2.9	1.9	1	0.7	0.8	6	4.4	1.3
Unknown	210	3.1	3	1.4	1.2	1	0.5	0.5	8	3.8	6.5	11	5.2	2.4
HIV risk behavior ^c														
MSM	2652	39.2	196	7.4	78.4	181	6.8	85.4	109	4.1	88.6	365	13.8	80.9
HRH	1989	29.4	23	1.2	9.2	11	0.6	5.2	4	0.2	3.3	35	1.8	7.8
IDU	452	6.7	1	0.2	0.4	1	0.2	0.5	0	0.0	0.0	2	0.4	0.4
Other	354	5.2	11	3.1	4.4	8	2.3	3.8	0	0.0	0.0	14	4.0	3.1
Unknown	1315	19.4	19	1.4	7.6	11	0.8	5.2	10	0.8	8.1	35	2.7	7.8
Nadir CD4 cell count, cells/mm ^{3d}														
<50	1056	15.6	17	1.6	6.8	17	1.6	8.0	9	0.9	7.3	37	3.5	8.2
50–199	1452	21.5	38	2.6	15.2	35	2.4	16.5	30	2.1	24.4	81	5.6	18.0
200–349	1703	25.2	74	4.3	29.6	72	4.2	34.0	34	2.0	27.6	137	8.0	30.4
350–499	1265	18.7	63	5.0	25.2	46	3.6	21.7	32	2.5	26.0	107	8.5	23.7
500+	1279	18.9	58	4.5	23.2	42	3.3	19.8	17	1.3	13.8	88	6.9	19.5
Housing at index date ^e														
Permanent/stable	4486	66.3	152	3.4	60.8	124	2.8	58.5	86	1.9	69.9	281	6.3	62.3
Temporary/unstable/homeless	530	7.8	29	5.5	11.6	31	5.8	14.6	17	3.2	13.8	59	11.1	13.1
Other	15	0.2	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Unknown	1731	25.6	69	4.0	27.6	57	3.3	26.9	20	1.2	16.3	111	6.4	24.6
Primary insurance at consent ^f														
Public	4313	63.8	137	3.2	54.8	119	2.8	56.1	56	1.3	45.5	239	5.5	53.0
Private	1819	26.9	72	4.0	28.8	60	3.3	28.3	54	3.0	43.9	143	7.9	31.7
Other	427	6.3	19	4.4	7.6	11	2.6	5.2	9	2.1	7.3	34	8.0	7.5
Unknown	203	3.0	22	10.8	8.8	22	10.8	10.4	4	2.0	3.3	35	17.2	7.8
Alcohol use at consent														
Yes	906	13.4	49	5.4	19.6	42	4.6	19.8	23	2.5	18.7	89	9.8	19.7
No	4149	61.4	104	2.5	41.6	83	2.0	39.2	45	1.1	36.6	193	4.7	42.8
Unknown	1707	25.2	97	5.7	38.8	87	5.1	41.0	55	3.2	44.7	169	9.9	37.5
Substance abuse at consent														
Yes	822	12.2	54	6.6	21.6	49	6.0	23.1	24	2.9	19.5	87	10.6	19.3
No	3787	56.0	97	2.6	38.8	73	1.9	34.4	52	1.4	42.3	178	4.7	39.5
Unknown	2153	31.8	99	4.6	39.6	90	4.2	42.5	47	2.2	38.2	186	8.6	41.2
Diagnoses of mental health conditions at consent ^g														
Ever HBV infection prior to consent	379	5.6	13	3.4	5.2	8	2.1	3.8	10	2.6	8.1	27	7.1	6.0
Ever HCV infection prior to consent	780	11.5	14	1.8	5.6	12	1.5	5.7	7	0.9	5.7	28	3.6	6.2

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HRH, heterosexual; IDU, injection drug user; IQR, interquartile range; MSM, men who have sex with men; STI, sexually transmitted infection.

^aAll characteristics are at the time of consent into the DC Cohort.

^bOther race/ethnicity includes persons of Asian/Pacific Island descent and those with more than 1 reported race.

^cHIV risk behaviors: HRH, IDU, MSM. MSM who are also IDUs are grouped with MSM. Other HIV transmission risk behavior includes persons who were perinatally infected or infected through blood transfusions, coagulation disorders, or occupational exposures.

^dNadir CD4 is the lowest CD4 record available dated prior to enrollment into the DC Cohort. Seven participants had an unknown nadir CD4 cell count.

^eTemporary/unstable housing was defined as a housing unit in which persons who are without housing or a fixed address receive temporary housing or shelter.

^fPublic insurance includes Medicare, Medicaid, and other public insurance coverage plans; "Other" insurance includes self-pay, recently terminated plans, clinical trial.

^gMental health conditions diagnosed previously or at the time of consent include major depressive disorder, anxiety disorder, bipolar disorder, psychoses, other.

Table 2A. Incidence Rates per 100 Person-Years of Chlamydia, Gonorrhea, and Syphilis^a by Baseline Demographic Characteristics^b Among DC Cohort Participants (n = 6762)

	Chlamydia	Gonorrhea	Syphilis	Any STI
	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)
Overall	1.8 (1.7–2.1)	1.7 (1.5–1.9)	0.8 (0.7–0.9)	3.8 (3.5–4.1)
Age at enrollment, y				
0–17	3.0 (1.7–5.3)	2.3 (1.2–4.4)	0.3 (0–1.8)	5.0 (3.3–7.8)
18–34	5.7 (5.0–6.6)	5.1 (4.4–5.9)	1.6 (1.2–2.1)	10.8 (9.7–12.0)
35–54	1.2 (1.0–1.5)	1.1 (0.9–1.3)	0.8 (0.7–1.0)	2.8 (2.5–3.2)
55+	0.2 (0.1–0.4)	0.3 (0.2–0.5)	0.2 (0.1–0.4)	0.6 (0.4–0.9)
Gender at consent				
Male	2.1 (1.9–2.4)	2.0 (1.8–2.3)	1.0 (0.9–1.2)	4.6 (4.2–5.0)
Female	0.7 (0.5–1.0)	0.4 (0.2–0.6)	0.1 (0–0.2)	1.1 (0.9–1.5)
Transgender female	5.1 (3.1–8.3)	3.8 (2.2–6.7)	1.6 (0.7–3.8)	9.9 (6.9–14.0)
Race/ethnicity				
Non-Hispanic black	1.7 (1.5–1.9)	1.4 (1.2–1.6)	0.6 (0.5–0.8)	3.3 (3.0–3.7)
Non-Hispanic white	2.5 (2.0–3.2)	2.6 (2.1–3.3)	1.2 (0.8–1.7)	5.3 (4.6–6.3)
Hispanic	4.2 (2.9–6.0)	4.4 (3.1–6.4)	1.9 (1.1–3.3)	9.2 (7.2–11.8)
Other	0.9 (0.3–2.8)	1.5 (0.6–3.7)	0.3 (0–2.2)	2.4 (1.2–4.9)
Unknown	0.5 (0.2–1.5)	0.2 (0–1.1)	1.5 (0.8–2.8)	2.1 (1.2–3.6)
HIV risk behavior				
MSM	3.6 (3.2–4.0)	3.6 (3.2–4.1)	1.7 (1.4–2.1)	7.7 (7.1–8.4)
HRH	0.5 (0.3–0.7)	0.2 (0.1–0.4)	0.1 (0–0.2)	0.8 (0.6–1.1)
IDU	0.1 (0–0.5)	0.1 (0–0.5)	NA	0.1 (0–0.6)
Other	1.6 (0.9–2.6)	1.0 (0.5–1.9)	NA	2.4 (1.6–3.7)
Unknown	0.8 (0.6–1.2)	0.4 (0.2–0.7)	0.3 (0.2–0.6)	1.5 (1.1–2.0)

Abbreviations: CI, confidence interval; HRH, heterosexual; IDU, injection drug user; MSM, men who have sex with men; NA, insufficient data for calculation; STI, sexually transmitted infection.

^aRate per 100 person-years of observation using Rothman/Greenland estimation for 95% confidence intervals.

^bAll characteristics are at the time of consent into the DC Cohort.

had public insurance and 26.9% had private insurance, 13.4 and 12.2% had a history of alcohol and substance abuse, respectively, and 11.5% had a hepatitis C diagnosis.

During a median follow-up period of 32.5 months, 6.7% of all participants developed an incident STI (n = 451); 3.7% of all participants had incident chlamydia infection (n = 250), 3.1% gonorrhea (n = 212), and 1.8% syphilis (n = 123). There was an additional 2.6% with possible incident syphilis that did not meet the definition of an incident case. Among participants with an incident STI, 30.4% had 2 or more STI episodes (n = 137); 19.3% had 2 STI episodes (n = 87), 7.3% had 3 (n = 33), 1.8% had 4 (n = 8), and 2.0% had 5–8 STI episodes (n = 9). Of all the STI episodes, 64.3% were among non-Hispanic blacks and 22.4% were among non-Hispanic whites. However, 5.6% of all enrolled non-Hispanic blacks developed an STI, whereas 10.7% of non-Hispanic whites and 13.7% of Hispanics developed an STI. Furthermore, 80.9% of individuals who developed an STI were MSM (Table 1).

The incidence rate of any STIs in the DC Cohort was 3.8 cases per 100 P-Y (95% CI, 3.5–4.1). The highest incidence rates of any STIs were noted in the following groups: age 18–34 years (10.8 cases per 100 P-Y; 95% CI, 9.7–12.0), transgender females (9.9 cases per 100 P-Y; 95% CI, 6.9–14.0), Hispanics (9.2 cases per 100 P-Y; 95% CI, 7.2–11.8), and MSM (7.7 cases per 100

P-Y; 95% CI, 7.1–8.4) (Table 2A). The STI incidence rates were stratified for race/ethnicity by age, gender, and risk behavior, as well as for age by risk behavior and gender. Taking into account the number of participants, the highest incidence rates were noted in transgender females age 18–34 years (21.0 cases per 100 P-Y; 95% CI, 14.0–31.0) and MSM age 18–34 years (15.0 cases per 100 P-Y; 95% CI, 14.0–17.0). Please refer to Table 2B for additional details.

In the univariate Poisson regression model, younger age, male gender, transgender women, non-Hispanic white and Hispanic race/ethnicity, MSM risk behavior, temporary/unstable housing, alcohol use, substance abuse, and higher nadir CD4 counts were all associated with a higher risk of developing an STI, while the presence of a mental health diagnosis and history of hepatitis C infection were associated with a lower risk (data not shown). In the multivariate Poisson regression model, younger age, especially 0–17 and 18–34 years, Hispanic ethnicity, MSM risk behavior, and higher nadir CD4 counts remained associated with a higher risk of developing an STI, while the presence of a mental health diagnosis was still associated with a lower risk (Table 3).

In the assessment of potential HIV transmission risk at the time of STI diagnosis, the VLs were assessed at ±1 month, 3 months, and 6 months (Table 4). VL measurements were not

Table 2B. Incidence Rates per 100 Person-Years of Chlamydia, Gonorrhea, and Syphilis^a by Baseline Demographic Characteristics^b Among DC Cohort Participants (n = 6762), Stratified for Race/Ethnicity by Age, Gender, and Risk Behavior

			Chlamydia	Gonorrhea	Syphilis	Any STI
		No.	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)
Stratify race/ethnicity by age, y						
Non-Hispanic black	0–17	131	3.5 (2.0–6.1)	2.6 (1.3–5.0)	0.3 (0.0–2.0)	5.8 (3.7–8.9)
	18–34	1057	5.7 (4.8–6.7)	4.9 (4.1–5.9)	1.5 (1.1–2.1)	10.8 (9.6–12.2)
	35–54	2732	0.9 (0.7–1.2)	0.7 (0.5–0.9)	0.6 (0.4–0.8)	2.0 (1.7–2.4)
	55+	1238	0.1 (0.0–0.3)	0.2 (0.1–0.4)	0.1 (0.0–0.2)	0.3 (0.2–0.6)
Non-Hispanic white	0–17	8	NA	NA	NA	NA
	18–34	141	7.8 (5.5–11.2)	7.3 (5.1–10.6)	1.6 (0.7–3.5)	13.1 (9.9–17.2)
	35–54	537	2.2 (1.6–3.0)	2.4 (1.7–3.3)	1.4 (1.0–2.2)	5.3 (4.3–6.6)
	55+	254	0.6 (0.3–1.5)	0.9 (0.4–1.8)	0.5 (0.2–1.3)	1.9 (1.1–3.1)
Hispanic	0–17	5	NA	NA	NA	NA
	18–34	89	6.7 (3.8–11.8)	7.2 (4.2–12.5)	1.1 (0.3–4.5)	13.4 (9.0–20.0)
	35–54	170	4.0 (2.5–6.6)	4.3 (2.7–6.9)	2.5 (1.4–4.7)	9.4 (6.8–13.0)
	55+	48	NA	NA	1.1 (0.2–8.1)	1.1 (0.2–8.1)
Stratify race/ethnicity by gender						
Non-Hispanic black	Male	3414	1.9 (1.7–2.2)	1.8 (1.5–2.1)	0.9 (0.7–1.1)	4.1 (3.7–4.5)
	Female	1648	0.8 (0.6–1.1)	0.4 (0.2–0.6)	0.1 (0.0–0.2)	1.2 (0.9–1.6)
	Transgender Female	96	6.1 (3.7–10.0)	3.4 (1.8–6.6)	1.9 (0.8–4.6)	10.7 (7.4–15.5)
Non-Hispanic white	Male	882	2.6 (2.1–3.3)	2.8 (2.2–3.5)	1.2 (0.9–1.8)	5.7 (4.8–6.7)
	Female	55	NA	NA	NA	NA
	Transgender Female	3	NA	NA	NA	NA
Hispanic	Male	270	4.7 (3.2–6.8)	4.7 (3.2–6.8)	2.2 (1.3–3.8)	10.1 (7.8–13.0)
	Female	31	NA	NA	NA	0.0 (0.0–)
	Transgender Female	11	NA	6.6 (1.6–26.2)	NA	6.6 (1.6–26.2)
Stratify race/ethnicity by risk behavior						
Non-Hispanic black	MSM	1620	3.8 (3.3–4.5)	3.6 (3.1–4.2)	1.7 (1.3–2.1)	8.1 (7.3–8.9)
	HRH	1792	0.5 (0.3–0.8)	0.2 (0.1–0.4)	0.1 (0.0–0.2)	0.8 (0.6–1.1)
	IDU	425	0.1 (0.0–0.6)	NA	NA	0.1 (0.0–0.6)
	Other	292	1.9 (1.1–3.3)	1.2 (0.6–2.4)	NA	3.0 (2.0–4.6)
	Unknown	1029	0.7 (0.4–1.1)	0.4 (0.2–0.8)	0.4 (0.2–0.7)	1.4 (1.0–2.0)
Non-Hispanic white	MSM	667	3.3 (2.6–4.2)	3.6 (2.9–4.6)	1.6 (1.1–2.3)	7.3 (6.2–8.6)
	HRH	58	NA	NA	NA	NA
	IDU	19	NA	NA	NA	NA
	Other	37	NA	NA	NA	NA
	Unknown	159	0.9 (0.3–2.3)	0.2 (0.0–1.5)	0.2 (0.0–1.5)	1.3 (0.6–2.9)
Hispanic	MSM	194	4.7 (3.1–7.2)	6.0 (4.2–8.7)	2.4 (1.3–4.3)	11.2 (8.5–14.7)
	HRH	57	1.0 (0.1–6.8)	NA	1.0 (0.1–6.8)	1.9 (0.5–7.7)
	IDU	4	NA	18.8 (2.7–133.6)	NA	18.8 (2.7–133.6)
	Other	9	NA	NA	NA	NA
	Unknown	48	6.7 (2.8–16.0)	1.3 (0.2–9.5)	1.3 (0.2–9.5)	9.3 (4.4–19.5)
Stratify age by risk behavior						
	MSM	5	24.0 (6.0–95.0)	24.0 (6.0–95.0)	12.0 (1.7–85.0)	48.0 (18.127.0)
	HRH	8	16.0 (5.1–49.0)	5.2 (0.7–37.0)	NA	21.0 (7.9–56.0)
	IDU	0	NA	NA	NA	NA
	Other	132	1.9 (0.9–4.1)	1.7 (0.7–3.7)	NA	3.3 (1.9–5.9)
0–17 y	Unknown	4	NA	NA	NA	NA
	MSM	796	7.7 (6.5–9.0)	7.8 (6.7–9.2)	2.4 (1.8–3.1)	15.0 (14.0–17.0)
	HRH	300	2.1 (1.3–3.4)	1.0 (0.5–2.0)	0.3 (0.1–1.1)	3.0 (2.0–4.6)
	IDU	5	NA	9.5 (1.3–67.0)	NA	9.5 (1.3–67.0)
18–34 y	Other	120	2.2 (1.0–4.8)	1.1 (0.3–3.3)	NA	3.2 (1.7–6.2)
	Unknown	155	5.5 (3.5–8.8)	1.5 (0.6–3.7)	1.2 (0.5–3.3)	8.0 (5.4–12.0)
	MSM	1433	2.5 (2.1–3.0)	2.4 (1.9–2.9)	1.8 (1.4–2.2)	5.9 (5.2–6.7)
	HRH	1200	0.3 (0.1–0.5)	0.1 (0.0–0.3)	0.1 (0.0–0.3)	0.5 (0.3–0.8)
	IDU	156	NA	NA	NA	NA
	Other	72	0.5 (0.1–3.8)	NA	NA	0.5 (0.1–3.8)

Table 2B. Continued

			Chlamydia	Gonorrhea	Syphilis	Any STI
		No.	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)	Rate (95% CI)
35–54 y	Unknown	772	0.3 (0.1–0.7)	0.3 (0.1–0.7)	0.3 (0.1–0.7)	0.8 (0.5–1.4)
	MSM	417	0.5 (0.2–1.1)	0.9 (0.5–1.7)	0.5 (0.2–1.1)	1.8 (1.1–2.7)
	HRH	481	NA	NA	0.1 (0.0–0.6)	0.1 (0.0–0.6)
	IDU	291	0.1 (0.0–0.8)	NA	NA	0.1 (0.0–0.8)
	Other	29	NA	NA	NA	NA
55+ y	Unknown	381	0.2 (0.1–0.9)	0.1 (0.0–0.8)	0.1 (0.0–0.8)	0.5 (0.2–1.2)
Stratify age by gender						
	Male	61	3.1 (1.3–7.5)	1.9 (0.6–5.8)	0.6 (0.1–4.4)	5.0 (2.5–10)
	Female	88	3.0 (1.4–6.2)	2.5 (1.1–5.6)	NA	5.1 (2.9–8.9)
0–17 y	Transgender female	0	NA	NA	NA	NA
	Male	993	6.6 (5.6–7.7)	6.2 (5.3–7.3)	2.0 (1.5–2.6)	13.0 (11–14)
18–34 y	Female	338	2.3 (1.5–3.7)	1.2 (0.6–2.2)	NA	3.3 (2.2–4.8)
	Transgender female	45	10 (5.7–18.0)	9.1 (5.1–16.0)	3.3 (1.2–8.8)	21.0 (14.0–31.0)
	Male	2552	1.5 (1.3–1.9)	1.5 (1.2–1.8)	1.1 (0.9–1.4)	3.7 (3.3–4.2)
35–54 y	Female	1024	0.3 (0.1–0.6)	0.1 (0.0–0.3)	0.1 (0.0–0.3)	0.4 (0.2–0.8)
	Transgender female	57	1.8 (0.6–5.6)	0.6 (0.1–4.3)	0.6 (0.1–4.3)	3.0 (1.2–7.2)
	Male	1217	0.2 (0.1–0.5)	0.4 (0.2–0.6)	0.2 (0.1–0.4)	0.7 (0.5–1.1)
55+ y	Female	371	NA	NA	0.1 (0.0–0.8)	0.1 (0.0–0.8)
	Transgender female	11	3.8 (0.5–27.0)	0.0 (0.0–0.0)	NA	3.8 (0.5–27)

Abbreviations: CI, confidence interval; HRH, heterosexual; IDU, injection drug user; MSM, men who have sex with men; NA, insufficient data for calculation; STI, sexually transmitted infection.

^aRate per 100 person-years of observation using Rothman/Greenland estimation for 95% confidence intervals.

^bAll characteristics are at the time of consent into the DC Cohort.

available for 116 (25.7%) participants at ±1 month, 44 (9.8%) at ±3 months, and 29 (6.4%) at ±6 months after STI diagnosis. Although VL measurements were missing for 25.7% of participants at the assessment closest to the STI episode, VL results were similar to those at 3 and 6 months and therefore assumed to be representative. Among individuals with any number of STI episodes, 41.8% had a detectable viral load (above the LLOQ) within 1 month of the STI diagnosis; 14.6% had a VL ≥1500 copies/mL. For those with 1 STI episode, 13.5% had a VL ≥1500 copies/mL and 7.4% had a VL ≥10 000 copies/mL. These percentages were higher in participants with 2 or more STI episodes; 17.1% had a VL ≥1500 copies/mL, and 13.3% had a VL ≥10 000 copies/mL. However, these differences did not achieve statistical significance.

DISCUSSION

In this large-scale, single city–focused analysis, we reported the incidence and factors associated with the development of chlamydia, gonorrhea, and syphilis in a cohort of people living with HIV (PLWH) in care in DC. Consistent with incidence rates among the DC general population [2], chlamydia had the highest incidence, followed by gonorrhea and then syphilis, each with particularly high rates among 18–34-year-olds, MSM, transgender women, and Hispanic participants.

Among age, gender, race/ethnicity, and risk categories, 18–34-year-olds, transgender women, Hispanics, and MSM had the highest STI incidence rates. In our stratified analysis,

the populations at particularly high risk included 18–34-year-olds of all races/ethnicities, MSM of all races/ethnicities, Hispanic men, and non-Hispanic black transgender women. All groups were at substantial risk of STIs, with incidence rates ranging from 7.3 to 13.4 cases per 100 P-Y. Although the overall number of transgender women enrolled in the DC Cohort was relatively low, at 113, this sample size afforded an opportunity for comparison of risk across the larger HIV-infected population overall and other high-risk populations. The very high risk of STIs identified among transgender women highlights the importance of strategies to reduce STI and HIV transmission that are culturally and gender sensitive across all at-risk groups.

In the multivariate analysis of factors associated with STI risk, younger age (especially <18 and 18–34 years), Hispanic ethnicity, MSM risk behavior, and higher nadir CD4 counts were strongly associated with a higher risk of developing an STI. It has been hypothesized that with higher CD4 counts (as a consequence of virologic suppression on ART), patients may perceive a lower “threat” of HIV transmission and therefore have higher-risk sexual behaviors [18–20]. To date, this association has not been proven [21–23], but our data on CD4 counts may suggest a potential association between improved general well-being and high-risk sexual behaviors. Certainly, it has been proposed that the greatest prevalence of STIs in PLWH is at the time of HIV diagnosis [24]. However, it is also widely recognized that high-risk sexual behaviors can continue at any point after

Table 3. Multivariate Poisson Regression Analysis for Factors Associated With the Development of STIs Among Participants in the DC Cohort

Participant Characteristic	Chlamydia		Gonorrhea		Syphilis		Any STI	
	RR (95% CI)	<i>P</i> ^a	RR (95% CI)	<i>P</i>	RR (95% CI)	<i>P</i>	RR (95% CI)	<i>P</i>
Age at consent, y								
0–17	24.2 (7.3–80.4)	<.0001	23.5 (7.2–76.6)	<.0001	2.5 (0.3–20.1)	.40	17.6 (7.2–42.9)	<.0001
18–34	15.7 (7.9–31.4)	<.0001	9.9 (5.4–18.2)	<.0001	6.1 (2.8–13.2)	<.0001	9.4 (6.2–14.1)	<.0001
35–54	4.4 (2.2–8.8)	<.0001	2.9 (1.6–5.2)	.001	3.9 (1.8–8.1)	.000	3.3 (2.2–4.9)	<.0001
55+	Ref		Ref		Ref		Ref	
Gender at consent^a								
Male	Ref		Ref		Ref		Ref	
Female	0.8 (0.5–1.3)	.385	0.6 (0.4–1.2)	.143	0.1 (0–0.3)	<.0001	0.7 (0.5–1)	.0316
Transgender female	1.3 (0.8–2.2)	.335	1 (0.5–1.8)	.945	1.3 (0.5–3.3)	.53	1.2 (0.8–1.8)	.3053
Race/ethnicity								
Non-Hispanic black	Ref		Ref		Ref		Ref	
Non-Hispanic white	1.3 (0.9–1.7)	.12	1.5 (1.1–2)	.009	1.3 (0.8–2)	.23	1.2 (1–1.5)	.05
Hispanic	1.4 (0.9–2.1)	.130	1.7 (1.1–2.5)	.009	1.7 (0.9–3)	.095	1.5 (1.1–1.9)	.008
Other	0.5 (0.2–1.5)	.21	1 (0.4–2.4)	.95	0.4 (0.1–2.7)	.33	0.6 (0.3–1.2)	.18
HIV risk behavior^b								
MSM	Ref		Ref		Ref		Ref	
HRH	0.3 (0.2–0.4)	<.0001	0.1 (0.1–0.3)	<.0001	1.3 (0.7–2.4)	.325	0.2 (0.1–0.3)	<.0001
IDU	0.1 (0–1.4)	.088	0.1 (0–1)	.045	0.2 (0–0.8)	.022	0.1 (0–0.7)	.03
Other	0.3 (0.1–0.8)	.02	0.2 (0–0.5)	.001	0.6 (0.4–0.9)	.01	0.2 (0.1–0.5)	<.001
Housing at consent^c								
Permanent/stable	Ref		Ref		Ref		Ref	
Temporary/unstable	1 (0.7–1.5)	.84	1.2 (0.8–1.9)	.29	1.8 (0.9–3.5)	.12	1.2 (1–1.6)	.089
Homeless	0.9 (0.4–2.3)	.88	1.5 (0.4–6.3)	.54	1.6 (0.9–2.6)	.08	0.8 (0.4–1.6)	.52
Primary insurance^d								
Public	1.3 (1–1.8)	.039	1.5 (1.1–2)	.020	1.3 (0.7–2.3)	.444	1.2 (1–1.5)	.062
Private	Ref		Ref		Ref		Ref	
Other	1.2 (0.6–2.4)	.576	0.7 (0.2–2)	.480	1.3 (0.7–2.5)	.374	1.2 (0.8–2)	.3727
Alcohol use	1.2 (0.8–1.9)	.320	1.2 (0.8–1.7)	.442	0.7 (0.4–1.4)	.355	1.2 (0.9–1.6)	.1598
Substance abuse	1.3 (0.8–2.1)	.194	1.4 (1–2)	.056	2.2 (1.1–4.4)	.034	1.3 (1–1.7)	.0345
Mental health diagnosis at consent ^e	0.3 (0.1–1)	.044	0.4 (0.1–1.1)	.072	2 (1–4)	.063	0.3 (0.1–0.6)	.0028
Ever HBV infection prior to consent	0.9 (0.5–1.5)	.631	0.7 (0.4–1.3)	.316	2.6 (1.3–5.2)	.009	0.9 (0.7–1.3)	.7119
Ever HCV infection prior to consent	1 (0.6–1.5)	.880	0.7 (0.4–1.2)	.215	1.8 (0.9–3.8)	.124	0.9 (0.7–1.3)	.5952
Nadir CD4 cell count^f								
<50	Ref		Ref		Ref		Ref	
50–199	1.5 (0.9–2.6)	.108	1.3 (0.8–2.2)	.29	1.3 (0.8–2.2)	.290	1.5 (1.1–2.1)	.017
200–349	2.6 (1.6–4.2)	<.0001	2.2 (1.4–3.5)	.001	2.2 (1.4–3.5)	.001	2.2 (1.6–3)	<.0001
350–499	2.2 (1.4–3.6)	.0015	1.8 (1.1–3)	.014	1.8 (1.1–3)	.014	1.9 (1.4–2.7)	<.0001
500+	2.4 (1.4–3.9)	.0007	1.7 (1.1–2.9)	.028	1.7 (1.1–2.9)	.03	1.9 (1.4–2.7)	.00

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HRH, heterosexual; IDU, injection drug user; MSM, men who have sex with men; Ref, reference group; RR, relative risk; STI, sexually transmitted infection.

^aTransgender men were not included in this analysis due to the small number (n = 5).

^bOther HIV transmission risk behavior includes persons who were perinatally infected or infected through blood transfusions, coagulation disorders, or occupational exposures.

^cTemporary/unstable housing was defined as a housing unit in which persons who are without housing or a fixed address receive temporary housing or shelter.

^dPublic insurance includes Medicare, Medicaid, and other public insurance coverage plans; "Other" insurance includes self-pay, recently terminated plans, clinical trial.

^eMental health conditions diagnosed previously or at the time of consent include major depressive disorder, anxiety disorder, bipolar disorder, psychoses, other.

^fNadir CD4 is the lowest CD4 record available dated prior to enrollment into the DC Cohort. Seven participants had an unknown nadir CD4 cell count.

^gA Bonferroni correction was applied to account for multiple testing, resulting in a significance level of .05/3 = .0167, and subsequent confidence intervals set at 98.33%.

HIV diagnosis [25, 26]. Thus, though risk may be reduced compared with before HIV diagnosis, this study demonstrates that ongoing STI and HIV transmission risk remains considerable.

There is significant heterogeneity between previous studies of STIs among PLWH in other large metropolitan areas of the United States [24]. Hence, the comparison between our STI prevalence (6.7% over a median follow-up of 32.5 months) and

incidence (3.8 cases per 100 P-Y) with other cohorts should be interpreted with caution. There are several studies that examine the incidence of bacterial STIs, but many of them focus on specific groups (eg, men, MSM, women) or settings (eg, STI clinics, military personnel). For example, a study on self-reported STIs via structured computer interviews in PLWH in Atlanta, Georgia, showed that 14% of respondents had an STI diagnosed

Table 4. HIV Viral Load in Participants With at Least 1 STI Episode (<LLOQ, LLOQ–<1500, 1500–<10 000, and ≥10 000 copies/mL) Within ±1 Month, ±3 Months, and ±6 Months of STI Diagnosis (n = 451)

Participants with at least 1 STI episode	Within 1 mo				Within 3 mo				Within 6 mo			
	<LLOQ	LLOQ–<1500	1500–9999	≥10 000	<LLOQ	LLOQ–<1500	1500–9999	≥10 000	<LLOQ	LLOQ–<1500	1500–9999	≥10 000
451	195 (58.2%)	91 (27.2%)	18 (5.4%)	31 (9.3%)	241 (59.4%)	108 (26.6%)	19 (4.7%)	38 (9.4%)	253 (60.0%)	112 (26.5%)	19 (4.5%)	38 (9.0%)

One hundred sixteen participants (25.7%) did not have a VL recorded within ±1 month, 44 participants (9.8%) did not have a VL recorded within ±3 months, and 29 (4.4%) participants did not have a VL recorded within ±6 months of STI diagnosis.

Abbreviations: LLOQ, lower limit of quantification; STI, sexually transmitted infection; VL, viral load.

in the previous 6 months, with a high frequency of STIs ever since HIV diagnosis (20% had chlamydia, 13% had gonorrhea, and 36% had syphilis) [25]. In contrast, in a cohort of HIV-infected Department of Defense beneficiaries, the prevalence of syphilis at the time of HIV diagnosis was 6%; the incidence rate was 1.3 cases per 100 P-Y [21]. As expected, published studies in which HIV-infected individuals were tested following STI screening protocols reported higher STI rates [27, 28] and are more likely to approach a true STI incidence.

Virologic suppression with antiretroviral therapy has been widely recognized as the key intervention to prevent HIV transmission, as recently confirmed in 2 large studies [11, 12]. There have been multiple attempts in the past to determine the extent to which STI control could impact HIV transmission, with mixed results [29–31]. Nevertheless, even when we fail to impact high-risk sexual behaviors, it is possible to interrupt HIV transmission if the VL is suppressed. Arguably the most important (and disappointing) finding of our analysis was the fact that 41.8% of participants with at least 1 STI episode had a detectable VL within 1 month of STI diagnosis. Furthermore, when using ≥1500 copies/mL as a proxy for transmission risk (albeit based on data in heterosexual transmission), 14.5% had ≥1500 copies/mL. Sustained virologic suppression among individuals with ongoing risk behaviors, signaled by the occurrence of an STI, may prevent HIV transmission from an infected sexual partner, and thus new HIV cases. Additionally, a notable finding from our data is the absence of VL measurement on 25.7% of those with STIs within ±1 month of STI diagnosis, 9.8% within ±3 months, and 6.4% at ±6 months. Yet our finding that 41.8% of participants within 1 month of STI diagnosis had a detectable VL should be an important reminder that presentation for STI evaluation is also a critical opportunity to address ART adherence and virologic suppression.

The DC Cohort database is linked semi-annually with the DC Department of Health (DC-DOH) HIV/AIDS surveillance database to enhance data accuracy, as individuals may receive care at multiple clinical sites. After completing our planned STI analyses, we examined linked data and found a 9.2% increase in the number of chlamydia cases (from 250 to 273 cases) and a 20.8% increase in the number of cases of gonorrhea (from 212 to 256 cases) during the period of study (unpublished data). These findings highlight that

linkage to care and virologic suppression opportunities may also require cross-site communication. We propose specifically that at each encounter for STI evaluation and/or treatment, even outside of the usual site of HIV care, a focused discussion and intensive efforts toward engagement in care and virologic suppression should be provided. This high-impact intervention among those potentially transmitting HIV not only provides profound individual benefit, but may also prevent new HIV cases in the community.

This study has several limitations. First, the observational nature of the DC Cohort precluded standardized STI screening for all participants. STIs are frequently asymptomatic, and differences in screening practices can impact the observed STI frequency [32, 33]. Subsequently, our reported STI incidence rates are likely underestimating the true STI incidence in PLWH in care in DC. Furthermore, STI screening may provide diagnosis dates distant from the actual time of STI acquisition with implications in our estimation of HIV transmission risk. Similarly, the study design also limited the availability of HIV VLs during the same encounter of STI diagnosis. Second, we were unable to distinguish genital or extragenital sites of chlamydia and gonorrhea infection. Third, the population enrolled in the DC Cohort may not be fully representative of the larger HIV-infected population in DC, as enrollment requires some degree of engagement in care, and the demographics of those declining consent differed slightly from those who provided consent.

Nonetheless, the strengths of this study include its city-wide, prospective enrollment of participants, its longitudinal study design, and the large sample size that is inclusive of male, female, and transgender participants. Also, our study is unique in linking data from multiple clinical sites with data reported to the local health department. Merging of the DC Cohort and the DC-DOH databases improved the accuracy of STI diagnosis frequency and provided insight into care received for STIs outside of the primary HIV care site. Finally, to our knowledge, this is the largest cohort to examine the occurrence of STIs and estimated HIV transmission risk in the DC metropolitan area, which has one of the highest incidence rates of HIV in the United States.

In conclusion, STIs are frequent among HIV-positive individuals receiving care in DC; thus risk reduction interventions are needed for people living with HIV to help control the spread of STIs, achieve durable HIV virologic suppression, and reduce

HIV transmission. These findings will help health care providers and policy makers provide high-impact interventions toward STI control and achievement of virologic suppression among PLWH with the goal of improving the health of the individual and reducing the incidence of HIV in the community.

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