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Rates of Sexually Transmitted Infection Diagnoses Among US Youth With Perinatally and Nonperinatally Acquired HIV

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Background: Of new sexually transmitted infections (STIs) in the United States, 50% occur among youth aged 15 to 24 years. Previous studies among youth with HIV (YHIV) do not distinguish STI trends among individuals with perinatally (YPHIV) and nonperinatally (YNPHIV) acquired HIV.

Methods: Among 3 Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) studies conducted between 2009 and 2015, we estimated incident diagnoses of trichomonal, bacterial, viral, and overall STIs stratified by sex assigned at birth, mode of HIV acquisition (perinatal [YPHIV] and nonperinatal [YNPHIV]), age (13–17 and 18–24 years), CD4 count (<200, 200–499, and ≥500/μL), and HIV viral load (VL) (<400 and ≥400 copies/mL).

Results: Among 3131 YHIV, across the 3 studies, mean (SD) age was 20.6 (2.6) years, 888 (28%) were female, 2498 (80%) had nonperinatal HIV acquisition recorded, and 2298 (73%) were African American/Black. Mean follow-up was 0.9 (0.3) years. Compared with YPHIV, YNPHIV spent less person-time with VL <400 copies/mL (47% vs. 53%) and more time off antiretroviral therapy (49% vs. 15%), and had higher overall STI rates (males, 65.9 vs. 8.5/100 person-years [PY]; females, 54.7 vs. 17.2/100 PY). Among YPHIV, bacterial STIs were higher during person-time spent with VL ≥400 vs. <400 copies/mL (male YPHIV, 10.9 vs. 0.6/100 PY; female YPHIV, 11.2 vs. 2.9/100 PY); no difference was observed among YNPHIV, which may be due to concurrent acquisition of HIV and other STIs and limited follow-up.

Conclusions: Compared with YPHIV, YNPHIV spent less time on antiretroviral therapy and virologically suppressed; YNPHIV also had higher STI diagnosis rates. Very high STI diagnosis rates among YHIV, including among those without virologic suppression, highlight the importance of youth-focused efforts to support durable virologic suppression and identify and treat STIs.

Fifty percent of new sexually transmitted infections (STIs) occur among youth aged 15 to 24 years in the United States.[1] Rates of STI diagnoses are increasing sharply nationwide, with *gonorrhea* and *syphilis* diagnoses increasing 67% and 76% from 2013 to 2017.[2] Several factors may be contributing, including declining school-based sexual education,[3] rising use of geosocial networking applications,[4] and changing STI screening practices (e.g., quarterly for individuals prescribed HIV preexposure prophylaxis [PrEP]).[5] Although sexual activity has decreased among adolescents overall over the last decade, barrier protection use among those who are sexually active has also declined.[6,7]

There is a substantial burden of STIs among youth with HIV (YHIV).[8–10] Studies of YHIV have found poorer HIV-related immune status to be a predisposing factor to increased STI susceptibility.[1,8,11–18] Coinfections of sexually transmitted infections also contributes to HIV transmission; both ulcerative and

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nonulcerative STIs may increase the risk of HIV transmission by increasing the concentration of HIV in semen, the urethra, and cervical fluid, as well as increasing HIV replication and shedding in the genital tract.[19,20] Inflammation may also lead to a disrupted mucosal barrier, facilitating transmission. The US Centers for Disease Control and Prevention estimates that among all people with HIV, the HIV transmission rate by age is highest from YHIV aged 13 to 24 years (5.1/100 person-years [PY]).[21] Although the degree to which concurrent STIs contribute to this HIV transmission is unknown, better understanding the burden of STI/HIV coinfection can inform interventions to increase STI screening and treatment among YHIV, impacting both the health of individual YHIV and onward HIV transmission. Notably, few studies of STIs among YHIV distinguish between youth with nonperinatally acquired HIV (YNPHIV) and perinatally acquired HIV (YPHIV), despite differences in sexual activity and age of sexual debut; one study of 752 YHIV found that among sexually active youth, YPHIV were less likely than YNPHIV to have been diagnosed with an STI in 2006.[9] Furthermore, there are no specific recommendations for YHIV, although there are STI screening guidelines for specific populations (e.g., as frequently as 3–6 monthly for young men who have sex with men).[22] Although HIV-specific guidelines recommend annual STI screening, the most recently released Centers for Disease Control and Prevention 2021 guidelines acknowledge that screening more frequently than annually may be appropriate based on local epidemiology and risk behaviors.[22]

Our objective was to analyze trichomonal, bacterial, and viral STI diagnosis rates stratified by sex and mode of HIV acquisition (perinatal and nonperinatal HIV), as well as age, CD4 count, and HIV viral load (VL). We used a large database from 3 studies conducted within the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), a US national clinical trials network. The 3 studies included data from more than 3000 individuals at 20 hospital- and community-based sites across the United States.[23,24] Given increased sexual activity among YNPHIV and older youth, we hypothesized that STI diagnosis rates would be higher among YNPHIV compared with YPHIV, older youth compared with younger youth, and those with poorer HIV-related immune status (lower CD4 counts and higher HIV VL) compared with those with improved HIV-related immune status (higher CD4 counts and lower HIV VL). These estimated STI diagnosis rates may provide important information to clinicians and health policymakers and help inform youth-focused interventions and/or youth-specific guidelines.

METHODS

Study Population

We analyzed data among 13- to 24-year-old YHIV from 2 cross-sectional studies (ATN 086, 106) and one longitudinal cohort study (ATN 125). ATN 086 and 106 were network-wide assessments of health status and behavioral risk factors. ATN 086 enrolled 1712 YPHIV and YNPHIV aged 12 to 24 years at 15 ATN sites between December 2009 and January 2011.[25] ATN 106 enrolled 513 YPHIV and YNPHIV aged 12 to 24 years at 5 ATN sites between June 2011 and June 2012.[26] ATN 125 was a network-wide assessment of the HIV care continuum. ATN 125 enrolled 924 YNPHIV aged 13 to 24 years at 14 ATN sites between March 2015 and December 2015 (Supplementary Methods and Supplementary Table 1, http://links.lww.com/OLQ/A772).[23] Twenty sites were both hospital and community based and were geographically diverse (Northeast, 3; South, 10; Midwest, 3; West, 3; Puerto Rico, 1).[23,24] Institutional review boards at participating sites approved each study. Demographic data were obtained via self-administered computer interviews. Although there was no simultaneous co-enrollment between protocols, we could not exclude later enrollment of 086/106 participants in ATN 125. We excluded 5 ATN 086 participants with missing STI diagnosis records. For the present analysis, deidentified data were obtained from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Data and Specimen Hub.

Clinical and Laboratory Data

For ATN 086/106, data were derived from a single study enrollment visit through chart extraction, including current antiretroviral (ARV) medications, 1 year of prior STI diagnoses, and the most recent VL and CD4 within the prior 6 months. Diagnoses were classified using the MedDRA classification system[27] and included *Trichomonas*, bacterial (*chlamydia*, *gonorrhea*, lymphogranuloma venereum, *Haemophilus ducreyi*, and syphilis) and viral (human papillomavirus, hepatitis B and C, and herpes simplex) diagnoses (Supplemental Digital Content, http://links.lww.com/OLQ/A772). For ATN 125, STI, CD4, and VL data were extracted from the medical record from 6 months before 6 months after enrollment or end of the ATN 125 study period. For all 3 studies, staff were instructed to list any new, ongoing, and resolved diagnoses; additional procedures have been described elsewhere for all 3 studies.[23,24]

Outcome Measures

We assessed the first occurrence of any STI diagnosis during the study period and categorized diagnoses as trichomonal, bacterial, or viral. Participants could contribute one event per category. Unless otherwise noted, we report a difference in point estimates when 95% confidence intervals (CIs) did not overlap.[28]

Statistical Analysis

We defined the study period for ATN 086/106 as from 1 year before enrollment through the enrollment date for ATN 086/106, and for ATN 125 as from 6 months before enrollment through study end.

Person-Time

To estimate the distribution of person-time, we stratified by mode of HIV acquisition (YPHIV vs. YNPHIV), age (13–17 and 18–24 years), CD4 count (<200, 200–499, and ≥500/μL), and HIV VL (VL <400 copies/mL and VL ≥400 copies/mL). When exact STI diagnosis dates were unavailable (for 697 [41%] ATN 086 and 508 [100%] ATN 106 participants), person-time was assigned as 1 year regardless of whether the participant experienced an event. Otherwise, person-time was determined by time to event or time to end of study. Because ATN 125 data were longitudinal, this study population was stratified by age and time-varying CD4 and VL, as in previous work.[17,29] We estimated dates when strata thresholds were crossed using linear interpolation between adjacent CD4 and $\log_{10}$VL measurements. The first available CD4 and VL measurements were carried backward to baseline, and the last available CD4 and VL measurements were carried forward until the end of follow-up. For ATN 086/106, baseline values were used for all stratification variables, and each participant contributed their entire person-time to exactly one stratum per variable. Because specific current ARV regimens at enrollment were available for ATN 086/106, for analyses restricted to these study populations, we additionally stratified by the combined measure of VL and ARV status. Based on guidelines and practice patterns during the study period, as in prior work, we defined combination antiretroviral therapy (cART) regimens as 1 of 3 mutually exclusive types expected to be suppressive: (1) ≥3

drugs from ≥2 classes, or (2) a protease inhibitor (excluding ritonavir alone) + 1 drug from another class, or (3) ≥3 nucleos(t)ide reverse transcriptase inhibitors.[30–35s] Although individual circumstances may justify alternative ART approaches, during the study period, they were not standard of care and were not expected to suppress VL.[30–35s] For ATN 125, specific ARV medications were not collected. In an additional analysis, we performed cross-tabulations for recent HIV diagnosis (within 6 months of study visit) versus currently on ARVs in studies 086/106.

Incidence of STI Diagnosis

Incidence rates of first STI diagnosis were estimated for strata defined by sex assigned at birth, mode of HIV acquisition, age, CD4, and VL. To account for instances when exact STI diagnosis dates were unavailable, incidence rates were estimated using exponential failure time models allowing for interval censored event times.[36s] Wald 95% CIs for stratum-specific rates were obtained from the fitted exponential models. Identical methods were used to obtain incidence rate estimates and associated 95% CIs for first bacterial, viral, and trichomonal STI diagnosis. Because diagnosis dates were available for ATN 125 participants, incidence rates restricted to this population were estimated using the person-time method (events/total PY) and corresponding 95% exact Poisson CIs were computed. For analyses restricted to ATN 086/106, the additional VL and ARV status stratification described previously were included.

Throughout the analysis, participants with missing CD4 or VL data were excluded from the respective stratum only. SAS 9.4 was used for all analyses.

RESULTS

Study Population Characteristics

Among 3131 YHIV across the 3 studies, mean (SD) age was 20.6 (2.6) years, 888 (28%) were female, 2498 (80%) had nonperinatal HIV acquisition recorded, and 2298 (73%) were African American/Black (Table 1). At baseline, mean (SD) CD4 was 530 (277)/μL and 1454 (46%) of participants had VL <400 copies/mL.

Among ATN 086/106 participants (for whom specific ARV and prescription dates were available, N = 2207), 1275 (58%) were prescribed cART at study enrollment (Table 1). Among ATN 086/106 participants, 444 (20%) were diagnosed with HIV ≤6 months before study enrollment; of these participants diagnosed ≤6 months before enrollment, 120 (27%) were prescribed some ARV therapy at the time of enrollment. Among the 1762 (80%) ATN 086/106 participants diagnosed >6 months before study enrollment, 1185 (67%) were prescribed ARV therapy at enrollment. More than half of YPHIV reported no sexual partners, whereas more than 80% of YNPHIV reported 1 or more sexual partners (ATN 086 and 106; Supplementary Table 2, http://links.lww.com/OLQ/A772). Condomless sex was most common among male YNPHIV (at least 93% of participants, ATN 086 and 106; Supplementary Table 3, http://links.lww.com/OLQ/A772).

Distribution of Person-Time

Compared with YPHIV, YNPHIV contributed the most person-time (77%) to the study. Although person-time was relatively evenly distributed across ages for YPHIV (13–17 years, 44%; 18–24 years, 56%), among YNPHIV, person-time was predominantly spent at older ages (13–17 years, 5%; 18–24 years, 95%; Table 2). Among YPHIV, older versus younger youth spent more person-time at CD4 <200/μL (13–17 years, 8%; 18–24 years, 24%) and with VL ≥400 copies/mL (13–17 years, 42%; 18–24 years, 51%; Supplementary Table 4, http://links.lww.com/OLQ/A772). In contrast, among YNPHIV, person-time spent at CD4 <200/μL was similar by age (13–17 years, 4%; 18–24 years, 8%), whereas

TABLE 1. Characteristics of ATN 086, ATN 106, and ATN 125 Participants

Characteristic	Participants* (n = 3131)
Study	
ATN 086	1699 (54)
ATN 106	508 (16)
ATN 125	924 (30)
Age at baseline, mean (SD), y	20.6 (2.6)
Female	888 (28)
Year of birth, mean (SD)	1991 (3)
Mode of HIV acquisition	
Perinatally acquired	633 (20)
Nonperinatally acquired	2498 (80)
Race†	
African American/Black	2298 (73)
White or other	775 (25)
Not reported	58 (2)
Ethnicity†	
Hispanic	559 (18)
Not reported	3 (0)
CD4 cell count at baseline, mean (SD), /μL	530 (277)
VL <400 copies/mL at baseline	1454 (46)
Treatment prescribed at baseline‡	
cART	1275 (58)
ARV therapy but not cART	31 (1)
No ARV therapy	901 (41)
Diagnosed with HIV ≤6 mo from study enrollment‡	444 (20)
On ARV therapy at enrollment	120 (27)
Diagnosed with HIV >6 mo from study enrollment‡	1762 (80)
On ARV therapy at enrollment	1185 (67)
CD4 cell counts per person per year during follow-up, mean (SD)	1.5 (1.0)
Viral loads per person per year during follow-up, mean (SD)	1.6 (1.2)
Prescribed any ARV regimens during study period§¶	763 (83)
Loss to follow-up‖	
ATN 086	1
ATN 106	0
ATN 125	5
Total person-years, mean (SD)	0.9 (0.3)

*n (%), unless otherwise indicated.

†ATN 086/106 participants reported exactly one race category (per questionnaire design). ATN 125 participants reported at least one, but possibly more than one race category (per questionnaire design). A total of 44 participants (1.4%) selected more than one race category; of these, 36 people selected "African American/Black" in addition to one or more other categories and were included in the "African American/Black" categories; all others were included in "White or other."

‡ATN 086/106 only. Antiretroviral status by time from HIV diagnosis date to study enrollment may be found in Supplementary Table 5, http://links.lww.com/OLQ/A772. Among ATN 125 participants, 763 (83%) were prescribed any ARV during the study period.

§ATN 125 only. For ATN 125 participants, presence or absence of ART medications was described, and specific antiretroviral medications were not available.

¶Study period was defined as follows: ATN 086/106, 1 year before enrollment through the enrollment date; ATN 125, 6 months before enrollment through the date when the participant left the study.

‖Loss to follow-up was defined as no data recorded for >12 months for any reason other than documented care transfer.

ARV indicates antiretroviral; ATN, Adolescent Medicine Trials Network for HIV/AIDS Interventions; cART, combination antiretroviral therapy; VL, viral load.

TABLE 2. Distribution of Person-Time Stratified by Mode of Transmission, Age, CD4 Count, and VL and ARV Status

	YPHIV		YNPHIV		Total	
Variable	Participants*, No. (%)	Person-Time, y (%)	No. (%) Participants*	Person-Time, y (%)	Participants*, No. (%)	Person-Time, y (%)
Total	633 (20)	623 (23)	2498 (80)	2078 (77)	3131 (100)	2,701 (100)
Age, y						
13–17	278 (44)	276 (44)	129 (5)	108 (5)	407 (13)	384 (14)
18–24	355 (56)	346 (56)	2369 (95)	1970 (95)	2724 (87)	2316 (86)
CD4 cell count, /μL†						
≥500	321 (51)	317 (51)	1318 (50)	1042 (51)	1639 (50)	1358 (51)
200–499	203 (32)	198 (32)	1132 (43)	870 (42)	1335 (41)	1069 (40)
<200	107 (17)	105 (17)	183 (7)	144 (7)	290 (9)	249 (9)
VL/ARV status (ATN 086/106 only, N = 2207)‡§						
Suppressive ARV therapy	320 (52)	315 (52)	552 (37)	480 (35)	872 (41)	795 (41)
Nonsuppressive cART	204 (33)	201 (33)	223 (15)	214 (16)	427 (20)	415 (21)
No ARV therapy	90 (15)	88 (15)	725 (48)	661 (49)	815 (39)	749 (38)
Viral load, copies/mL¶						
<400	334 (53)	329 (53)	1258 (48)	962 (47)	1592 (49)	1291 (48)
≥400	299 (47)	294 (47)	1380 (52)	1088 (53)	1679 (51)	1382 (52)

*Number of participants contributing person-time toward a given stratum. Participants may contribute person-time to more than one stratum.

†Five ATN 086/106 participants and 23 ATN 125 person-visits with no available CD4 count data were excluded from CD4 strata.

‡Does not include ATN 125 participants because specific antiretroviral medications were not available.

§Eighty-one participants in ATN 086/106 with VL <400 copies/mL and without recorded ARVs, and 6 participants with VL ≥400 copies/mL and currently prescribed an ARV regimen other than cART, were excluded from VL/ARV status strata.

¶Six ATN 086/106 participants and 27 ATN 125 person-visits with no available VL data were excluded from VL strata.

ARV indicates antiretroviral; cART, combination antiretroviral therapy; VL, viral load; YNPHIV, youth with HIV acquired nonperinatally; YPHIV, youth with HIV acquired perinatally.

younger youth spent more person-time with VL ≥400 copies/mL (13–17 years, 71%; 18–24 years, 52%; Supplementary Table 4, http://links.lww.com/OLQ/A772). The majority of YNPHIV person-time was spent between ages 18 and 24 years (86%) and with CD4 ≥500/μL (51%). In ATN 086/ATN 106, YNPHIV participants currently on suppressive ARVs contributed the most (41%) person-time compared with those on nonsuppressive cART (21%) and no ARVs (38%). Given the substantial person-time with no ARVs (38%), during which participants were viremic, we additionally examined ARV status based on time from HIV diagnosis to enrollment. Among ATN 086/106 participants currently off ARVs at the study visit (901 of 2207 [41%]), most (64%) received an HIV diagnosis >6 months before enrollment (Supplementary Table 5, http://links.lww.com/OLQ/A772).

First STI Diagnoses: Female Participants

Among female participants, there were 285 first STI events (38.3/100 PY; Table 3), 43% had ≥1 STI. Higher rates of STI diagnoses were observed in female YNPHIV versus YPHIV (54.7 vs. 17.2/100 PY; Table 3), including after stratifying by age (13–17 years, 60.8 vs. 7.4/100 PY; 18–24 years, 54.2 vs. 25.5/100 PY; Supplementary Table 6, http://links.lww.com/OLQ/A772), reported race (African American/Black, 54.8 vs. 20.1/100 PY; White or other, 54.7 vs. 9.8/100 PY; Supplementary Table 6, http://links.lww.com/OLQ/A772), and number of sexual partners (no sexual partners, 65.2 vs. 2.9/100 PY; ≥1 sexual partners, 62.0 vs. 33.2/100 PY; Supplementary Table 7, http://links.lww.com/OLQ/A772, 086/106 participants only). Among female YPHIV, higher rates of STI diagnoses were observed during person-time spent at older ages (13–17 years, 7.4/100 PY; 18–24 years, 25.5/100 PY), no difference was observed by CD4 or VL (Supplementary Table 6, http://links.lww.com/OLQ/A772; Fig. 1). Among female YNPHIV, higher rates of STI diagnoses were observed during person-time spent at CD4 <200/μL versus CD4 ≥500/μL (<200/μL, 103.5/100 PY; ≥500/μL, 48.4/100 PY); no difference was observed by age or VL (Supplementary Table 6, http://links.lww.com/OLQ/A772; Fig. 1).

First STI Diagnoses: Male Participants

Among male participants, there were 977 first STI events (56.8/100 PY) in ATN 086/106/125 (Table 3), 43% had ≥1 STI. Higher rates of STI diagnoses were observed in male YNPHIV versus YPHIV (65.9 vs. 8.5/100 PY; Table 3, Fig. 2), including after stratifying by age (13–17 years, 65.3 vs. 3.3/100 PY; 18–24 years, 65.9 vs. 13.0/100 PY; Supplementary Table 8, http://links.lww.com/OLQ/A772), reported race (African American/Black, 69.0 vs. 8.6/100 PY; White or other, 57.1 vs. 7.3/100 PY; Supplementary Table 8, http://links.lww.com/OLQ/A772), and number of sexual partners (no sexual partners, 47.4 vs. 2.7/100 PY; ≥1 sexual partners, 62.7 vs. 15.6/100 PY; Supplementary Table 9, http://links.lww.com/OLQ/A772, 086/106 participants only). Among male YPHIV, higher rates of STI diagnoses were observed during person-time spent at older ages, although CIs had a small degree of overlap (13–17 years, 3.3/100 PY [95% CI, 1.2–8.7]; 18–24 years, 13.0/100 PY [95% CI, 8.3–20.3]); no difference was observed by CD4 or VL (Supplementary Table 8, http://links.lww.com/OLQ/A772; Fig. 2). Among male YNPHIV, no difference was observed by age, CD4, or VL (Supplementary Table 8, http://links.lww.com/OLQ/A772; Fig. 2).

Trichomonal STI Diagnoses

Among female participants, there were 58 first trichomonal (7.8/100 PY) STI events (Table 3). Higher rates of trichomonal STI diagnoses were observed in YNPHIV versus YPHIV (12.1

TABLE 3. Incidence Rates for First Sexually Transmitted Infection Diagnosis Among Females and Males in ATN 086/106/125

Sex	STI	Mode of Acquisition	Person-Time, y	Events, No.	Incidence Rate, /100 PY	95% CI
Female*	Overall	Perinatal	342.8	56	17.2	13.2–22.4
		Nonperinatal	469.7	229	54.7	48.0–62.3
		Total	812.5	285	38.3	34.1–43.0
	Trichomonal	Perinatal	342.8	8	2.4	1.2–4.8
		Nonperinatal	469.7	50	12.1	9.2–16.0
		Total	812.5	58	7.8	6.0–10.1
	Bacterial	Perinatal	342.8	23	7.0	4.6–10.5
		Nonperinatal	469.7	121	28.9	24.1–34.5
		Total	812.5	144	19.2	16.3–22.6
	Viral	Perinatal	342.8	40	12.3	9.0–16.8
		Nonperinatal	469.7	123	30.7	25.7–36.7
		Total	812.5	163	22.5	19.3–26.2
Male†	Overall	Perinatal	279.8	23	8.5	5.7–12.8
		Nonperinatal	1608.4	954	65.9	61.8–70.3
		Total	1888.3	977	56.8	53.3–60.5
	Bacterial	Perinatal	279.8	14	5.1	3.0–8.6
		Nonperinatal	1608.4	746	51.6	48.0–55.5
		Total	1888.3	760	44.1	41.1–47.4
	Viral	Perinatal	279.8	11	4.0	2.2–7.3
		Nonperinatal	1608.4	347	25.6	23.0–28.4
		Total	1888.3	358	21.9	19.8–24.3

*Among female participants, 43% had ≥1 STI. Of those who had a bacterial STI event, 57% had a chlamydia diagnosis; of those who had a viral STI event, 55% had an HPV diagnosis.

†Among male participants, 43% had ≥1 STI. Of those who had a bacterial STI event, 55% had a syphilis diagnosis; of those who had a viral STI event, 68% had an HPV diagnosis.

ATN indicates Adolescent Medicine Trials Network for HIV/AIDS Interventions; CI, confidence interval; PY, person-year; STI, sexually transmitted infection.

vs. 2.4/100 PY), including when accounting for differences in age distribution (Table 3; Supplementary Table 10, http://links.lww.com/OLQ/A772). Among female YNPHIV and YPHIV, no difference in trichomonal STI diagnoses was observed by age, CD4, or VL (Supplementary Table 10, http://links.lww.com/OLQ/A772).

Bacterial STI Diagnoses

Among female participants, there were 144 first bacterial (19.2/100 PY) STI events; 57% of these participants had a chlamydia diagnosis (Table 3). Among female participants, higher rates of bacterial STI diagnoses were observed in YNPHIV versus YPHIV (28.9 vs. 7.0/100 PY; Table 3). Among female YPHIV, higher rates of bacterial STIs were observed during person-time spent at higher VLs, although CIs had a small degree of overlap (≥400 copies/mL, 11.2/100 PY [95% CI, 7.1–17.8]; <400 copies/mL, 2.9/100 PY [95% CI, 1.2–7.1]); no difference was observed by age or CD4 (Supplementary Table 11, http://links.lww.com/OLQ/A772). Among female YNPHIV, no difference was observed by age, CD4, or VL (Supplementary Table 11, http://links.lww.com/OLQ/A772).

Among male participants in ATN 086/106/125, there were 760 first bacterial (44.1/100 PY) STI events; 55% of these participants had a syphilis diagnosis (Table 3). Among male participants, higher rates of bacterial STI diagnoses were observed in YNPHIV versus YPHIV (51.6 vs. 5.1/100 PY; Table 3). Among male YPHIV, higher rates of bacterial STI diagnoses were observed during person-time spent at VL ≥400 copies/mL (10.9/100 PY vs. 0.6/100 PY; Supplementary Table 12, http://links.lww.com/OLQ/A772); no difference was observed by age or CD4. Among male YNPHIV, no difference in bacterial STI diagnoses was observed by age, CD4, or VL (Supplementary Table 12, http://links.lww.com/OLQ/A772).

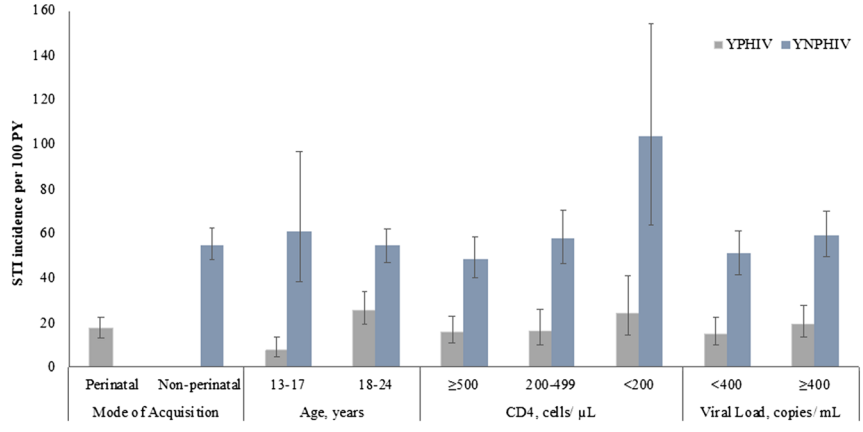

Figure 1. Incidence of first STI diagnosis among female YHIV in ATN 086/106/125 during the study period. Error bars indicate 95% CIs.

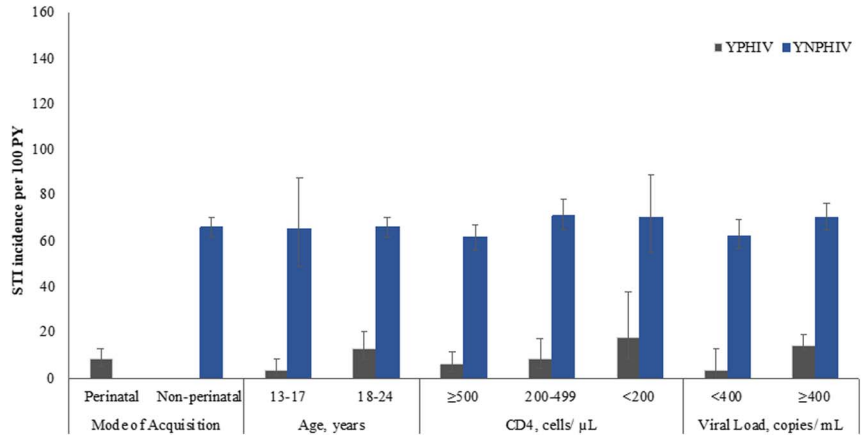

Figure 2. Incidence of first STI diagnosis among male YHIV in ATN 086/106/125 during the study period. Error bars indicate 95% CIs.

Viral STI Diagnoses

Among female participants, there were 163 first viral (22.5/100 PY) STI events; 55% of these participants had a human papillomavirus (HPV) diagnosis (Table 3). Among female participants, higher rates of viral STI diagnoses were observed in YNPHIV versus YPHIV (30.7 vs. 12.3/100 PY; Table 3). Among female YPHIV, higher rates of viral STI diagnoses were observed during person-time spent at older ages (13–17 years, 3.4/100 PY; 18–24 years, 19.8/100 PY); no difference was observed by CD4 or VL (Supplementary Table 13, http://links.lww.com/OLQ/A772). In contrast to YPHIV, among female YNPHIV, higher rates of viral STI diagnoses were observed during person-time spent at CD4 <200/µL versus CD4 ≥200/µL (<200/µL, 80.8/100 PY; 200–499/µL, 30.5/100 PY; ≥500/µL, 26.1/100 PY); no difference was observed by age or VL (Supplementary Table 13, http://links.lww.com/OLQ/A772).

Among male participants in ATN 086/106/125, there were 358 first viral (21.9/100 PY) STI events; 68% of these participants had an HPV diagnosis (Table 3). Among male participants, higher rates of viral STI diagnoses were observed in YNPHIV versus YPHIV (25.6 vs. 4.0/100 PY; Table 3). Among male YPHIV, no difference in viral STI diagnoses was observed by age, CD4, or VL (Supplementary Table 14, http://links.lww.com/OLQ/A772). Among male YNPHIV, higher rates of viral STI diagnoses were observed during person-time spent at CD4 <200/µL versus CD4 ≥500/µL; however, CIs had a small degree of overlap (<200/µL, 38.3/100 PY [95% CI, 27.3–53.6]; ≥500/µL, 23.3/100 PY [95% CI, 19.9–27.3]); no difference was observed by age or VL (Supplementary Table 14, http://links.lww.com/OLQ/A772).

DISCUSSION

To our knowledge, this is the largest study to date reporting STI diagnoses rates among YHIV aged 13 to 24 years, stratified by age, mode of HIV acquisition, CD4 count, and VL. These findings, based on data from studies conducted from 2009 to 2015, build on those of a study of 2006 data with a sample size approximately one-third that of the present analysis.[9] This analysis had 3 key findings. First, both YPHIV and YNPHIV spent substantial time without virologic suppression, which may lead to lower CD4 counts and poorer health outcomes. Consistent with previous publications, older YPHIV aged 18 to 24 years spent more person-time at lower CD4 compared with participants aged 13 to 17 years.[17,29,37s] We did not observe a pattern of change in person-time spent in CD4 strata by age among YNPHIV; this may be due to the small amount of person-time contributed by YNPHIV participants aged 13 to 17 versus 18 to 24 years (5% vs. 95%), as well as not explicitly accounting for time since HIV diagnosis. However, YNPHIV aged 18 to 24 years spent an increased proportion of person-time virologically suppressed compared with those aged 13 to 17 years (48% vs. 29%). Among YNPHIV who were not currently on ARVs at the time of study visit, most (64%) had been diagnosed more than 6 months before study enrollment. The substantial person-time spent off ARV therapy among YNPHIV is consistent with previous ATN reports[24] but is considerably higher than reported in the HIV Research Network (13–17 years, 2%; 18–24 years, 10%) during a similar period[29]; this finding may reflect differences in follow-up duration, study populations, or study sites (e.g., youth-focused services or insurance coverage)[38s] leading to increased time to initiate ARV therapy or other barriers to ARV use.[39s,40s] These data highlight the potential value of immediate ART initiation in youth newly diagnosed with HIV, which has been demonstrated in adult US populations to reduce time to virologic suppression.[40s–44s]

Second, given increased sexual activity among YNPHIV,[7] YNPHIV were at higher risk for STIs compared with YPHIV; these findings persisted when stratified by age, race, or number of sexual partners. Among YPHIV, we report similar STI diagnosis rates (female, 5.8/100 PY; male, 0.9/100 PY) compared with the Pediatric HIV/AIDS Cohort Study and the International Maternal Pediatric Adolescent HIV/AIDS Network (female and male, 4.7 and 0.6/100 PY with ages 13–30 years).[17] Among YNPHIV aged 13 to 17 years (female, 19.3/100 PY; male, 21.6/100 PY), our rates are similar to those reported in an ATN PrEP study (men who have sex with men aged 15 to 17 years [9.4–18.1/100 PY]);[45s] notably, reported STI diagnosis rates are lower among young than adult male PrEP users.[46s] National STI rates among youth aged 15 to 24 years (including recurrence) in 2018 were far lower for female and male individuals: 3.7 and 1.4/100 PY for chlamydia, 0.6 and 0.5/100 PY for gonorrhea, and 0.001 and 0.03/100 PY for syphilis. Although we report a different, combined measure of first occurrence of bacterial STI diagnoses among YHIV aged 13 to 24 years (males, 44.1/100 PY; females, 19.2/100 PY), our results suggest a higher burden of STIs among YHIV acquired either perinatally or nonperinatally compared with national averages.[47s] High rates of STI diagnoses among YNPHIV compared with YPHIV[48s] and among YHIV compared with youth nationwide underscore the need to provide comprehensive sexual health care for YHIV. Notably, 73% of the cohort identified as African American/Black, populations that are also disproportionately impacted by STIs.[49s] These data support the need to evaluate innovative youth-focused approaches to prevention and treatment of STIs among YHIV, such as extended clinic hours, drop-in, and self- and anonymous STI testing.[50s–52s]

Third, we observed higher overall STI rates among older female YPHIV aged 18 to 24 years (18–24 years, 25.5/100 PY; 13–17 years, 7.4/100PY); this is consistent with the observation that YPHIV are less likely to be sexually active than their peers at younger ages.[53s,54s] However, no such differences were observed among YNPHIV, perhaps because of concurrent acquisition of HIV with other STIs and high overall STI rates. A national study observed that YNPHIV were more frequently sexually active compared with YPHIV (89% vs. 34%).[9] YNPHIV had more episodes of condomless sex and sex partners compared with YPHIV[24]—sexual behaviors that put YNPHIV at risk for additional STIs.[55s] Given the burden of STIs, in particular among YNPHIV, these data support consideration for guidelines permitting more frequent routine STI screening among YNPHIV, as have been made for other special populations (e.g., as frequently as 3–6 monthly for young men who have sex with men).[22]

However, not all our hypotheses were demonstrated in this exploratory study. Given data linking higher STI rates with poorer HIV-related immune status,[8,11–17,56s] we hypothesized that those with lower CD4 and higher VL would have higher overall STI diagnosis rates compared with those with better immune status. Although we observed higher overall STI diagnosis rates at lower CD4 among female YNPHIV, no such differences were observed in male YNPHIV, perhaps because of high rates of STI diagnoses among male YNPHIV at all VL and CD4 counts, or concurrent acquisition of HIV and other STIs. However, there were key differences in the stratified STI diagnoses among YPHIV and YNPHIV: higher rates of bacterial STI diagnoses were observed among YPHIV with higher than with lower VL. This pattern was not observed among YNPHIV, possibly because of higher rates of bacterial STI diagnoses regardless of VL status. In addition, higher rates of viral STI diagnoses were observed among YNPHIV with lower versus higher CD4, and this may reflect viral reactivation at lower CD4 in the setting of high rates of overall viral STI rates; in contrast, this was not observed in YPHIV, potentially because of small numbers. Participants in all studies were cared for at YHIV-focused adolescent/young adult clinics; risk assessment was standard clinical care and drove frequency and type of STI testing and thus diagnosis. Few studies compare YPHIV and YNPHIV,[9] and none, to our knowledge, stratify by age, time-updated CD4 count, and VL.

This analysis had several limitations, including those that may have led us to either overestimate or underestimate STI rates. First, STI diagnosis rates among YNPHIV may have been subject to misclassification bias: given that the timing of infection was unknown and YNPHIV may have acquired STIs either concurrently or temporally proximal to HIV acquisition; however, our rates are similar to those reported in youth at risk for acquiring HIV.[45s] Second, we used data from 2 different study designs with a 1-year follow-up period; missing diagnosis dates for several participants precluded exact determination of person-time at risk and may have underestimated STIs. Conversely, although there was no simultaneous co-enrollment between protocols, we could not exclude later enrollment of 086/106 participants in ATN 125, which could have led to either an underestimation or overestimation of rates. Third, we were unable to distinguish between STIs that were detected because of symptoms versus routine screening or by anatomic site. In addition, ATN 125 was conducted in 2015 after PrEP guidelines were first issued in 2014, which may have led to increased STI screening practices in general. Finally, these data do not reflect the burden of STI infection among YHIV not engaged in HIV care; YHIV have lower retention than any other population.[57s] In addition, STI rates are high among people with HIV who are not retained in HIV care.[58s] Our findings—when appreciated within the context of a population engaged in care—provide meaningful estimates of STI rates by mode of HIV acquisition; despite potential error in our incidence rate estimates, these data support that YHIV, especially YNPHIV, are at an increased risk for STIs when compared with the general population.

In conclusion, compared with YPHIV, YNPHIV spent less time both on ART and virologically suppressed, and had higher rates of STIs. Very high rates of STIs among YHIV, including among those without virologic suppression, highlight the important of youth-focused efforts to support durable virologic suppression and identify and treat STIs.

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For further references, please see "Supplemental References," http://links.lww.com/OLQ/A773.