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MAJOR ARTICLE

Anatomic Site–Specific Gonorrhea and Chlamydia Testing and Incidence Among People With HIV Engaged in Care at 4 US Clinical Centers, 2014–2018

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Background. The incidence of *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) is increasing in the United States; however, there are limited data on anatomic site–specific GC/CT among people with HIV (PWH).

Methods. We reviewed records of all PWH in care between January 1, 2014, and November 16, 2018, at 4 sites in the CFAR Network of Integrated Clinical Systems Cohort (CNICS; n = 8455). We calculated anatomic site–specific GC/CT testing and incidence rates and used Cox proportional hazards models modified for recurrent events to examine sociodemographic and clinical predictors of GC/CT testing and incidence at urogenital, rectal, and pharyngeal sites. We also calculated site-specific number needed to test (NNT) to detect a positive GC/CT test.

Results. Of 8455 PWH, 2460 (29.1%) had at least yearly GC/CT testing at any anatomic site. The rates of urogenital, rectal, and pharyngeal GC were 1.7 (95% CI, 1.6–1.9), 3.2 (95% CI, 3.0–3.5), and 2.7 (95% CI, 2.5–2.9) infections per 100 person-years, respectively. The rates of urogenital, rectal, and pharyngeal CT were 1.9 (95% CI, 1.7–2.1), 4.3 (95% CI, 4.0–4.5), and 0.9 (95% CI, 0.8–1.0) infections per 100 person-years, respectively. PWH 16–39 years old experienced greater GC/CT rates at all anatomic sites, while men who have sex with men experienced greater rates of extragenital infections. NNTs for urogenital, rectal, and pharyngeal GC/CT were 20 (95% CI, 19–21), 5 (95% CI, 5–5), and 9 (95% CI, 8–9), respectively.

Conclusions. Many PWH are not tested annually for GC/CT, and rates of GC/CT infection, particularly rates of extragenital infections, are high. We identified groups of PWH who may benefit from increased site-specific GC/CT testing.

Keywords. gonorrhea; chlamydia; testing; incidence; people with HIV.

The Centers for Disease Control and Prevention (CDC) recommends yearly testing for either screening or diagnostic purposes for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) among sexually active people with HIV (PWH), with more frequent testing based on risk [1]. However, prior evaluations of sexually transmitted infection (STI) screening among PWH have indicated that GC/CT testing has fallen short of these recommendations [2, 3].

Concurrently, the incidence of diagnosed infections caused by *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) is increasing in the United States [4]. While there are limited data on the epidemiology of GC and CT among people with HIV (PWH), recent clinical cohort data indicate a concurrent increase in the incidence of GC and CT over the past 5–10 years [3, 5, 6]. One shortcoming of the available data is that the incidence of GC and CT is often reported in aggregate rather than by anatomic site. Men who have sex with men (MSM) experience extragenital infections at rates greater than urogenital infections [7], and among cisgender women with extragenital exposures, the prevalence of rectal GC may be greater than that of urogenital GC [8]. Correlates of incident GC and/or CT (GC/CT) infections likely differ by anatomic site, and infections at different anatomic sites may have differential implications for GC/CT transmission and the transmission of HIV [9, 10] and other sexually transmitted infections (STIs), like syphilis [11] and hepatitis C virus (HCV) [12]. For example, anogenital infections are more likely to potentiate HIV transmission than pharyngeal infections.

The anatomic site of GC and CT has important implications for treatment, follow-up, and antimicrobial resistance. For example, pharyngeal GC is more difficult to cure than urogenital GC, sustains population-level transmission of GC, and acquires resistance mutations from commensal *Neisseria* species [13–18]. In addition, higher doses of ceftriaxone may be

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required to sustain drug levels above minimum inhibitory concentrations (MICs) for a greater duration in pharyngeal tissue [19]. In the context of rapidly rising incidence of elevated MICs, a single dose of ceftriaxone 500 mg IM for people weighing <150 kg and 1000 mg IM for those weighing ≥150 kg is now the recommended treatment for pharyngeal GC, with a test of cure at 7–14 days to confirm eradication [15]. For rectal CT, doxycycline is now the established standard of care [20, 21].

We sought to estimate the rates of anatomic site–specific GC/CT testing for screening and diagnostic purposes and assess sociodemographic and clinical predictors of site-specific GC/CT testing among PWH in a national prospective clinical cohort. To assess the burden of GC/CT infections and determine priority populations for GC/CT testing, we estimated the incidence of diagnosed urogenital, rectal, and pharyngeal GC/CT and examined sociodemographic and clinical correlates of GC/CT infections at each anatomic site. In addition, we calculated the number needed to test (NNT) to detect a GC/CT infection at each anatomic site to further identify PWH who may benefit from increased testing and behavioral and biomedical STI prevention [22–25].

METHODS

Data Source

The Centers for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS) is a dynamic prospective observational cohort study of adult PWH in routine clinical care at 8 academic institutions across the United States; methods of data collection have been previously reported [26]. Briefly, comprehensive clinical data collected through electronic medical records and other institutional data systems undergo rigorous data quality assessment and are harmonized in a central data repository that is updated quarterly.

We studied all PWH with at least 1 year of follow-up beginning on or after January 1, 2014, through November 16, 2018, with at least 1 clinic visit or viral load or CD4 count in each calendar year of follow-up at 4 CNICS sites with relevant data available at the time of analysis: Fenway Community Health/Harvard Medical School, Boston, MA, USA; Johns Hopkins University, Baltimore, MD, USA; University of Washington, Seattle, WA, USA; and University of California–San Diego, San Diego, CA, USA. Participant follow-up time was divided into 3-month intervals to reduce bias introduced by participants with very frequent visits (median [range], 13 [2–48]), as follow-up frequency may be associated with more frequent testing for and diagnosis of GC/CT, and to mirror intervals recommended by the CDC for STI testing and follow-up [1]. The observation period ended with the earliest of occurrence of death, last date of voluntary CNICS participation, or November 16, 2018.

Patient Consent

All CNICS participants provided written informed consent for study participation. CNICS research was approved by institutional review boards at each clinical site.

Outcomes

For testing analyses, we examined the binary outcomes of receipt of nucleic acid amplification tests (NAATs) for GC/CT at urogenital (urine, vaginal, or cervical specimens), rectal, or pharyngeal sites. Each of the 4 CNICS sites used GC/CT NAATs internally validated for each anatomic site at their respective reference laboratories (Aptima Combo 2 Assay, Hologic, Inc., Marlborough, MA, USA [University of Washington and Fenway Community Health], and cobas CT/NG, Roche Diagnostics, Indianapolis, IN, USA [Johns Hopkins University and University of California–San Diego]).

The University of Washington [27] and Fenway Community Health (K.H. Mayer, personal communication, May 20, 2022) implemented 3-site GC/CT self-testing before and during the entire study period. Concurrently, Fenway Community Health had a bundled STI order set in the electronic medical record (EMR) that included orders for GC/CT NAATs at urogenital, rectal, and pharyngeal sites. University of California–San Diego initiated clinic-wide GC/CT self-testing in 2016 in addition to routine 3-site GC/CT testing for patients attending high-resolution anoscopy clinics and for patients with HCV before, during, and after direct-acting antiviral therapy through 12-week sustained virologic response (E. Cachay, personal communication, May 23, 2022). From 2013 to 2015, Johns Hopkins implemented a pop-up reminder in the EMR for providers to test for GC/CT if testing had not been done in the prior 11 months with a direct link to an order for a urogenital GC/CT NAAT and a prompt to consider extragenital testing (S. Berry, personal communication, May 24, 2022).

For incidence analyses, we examined the binary outcomes of the results of GC/CT NAATs at urogenital, rectal, and pharyngeal sites.

Covariates

Sociodemographic Characteristics

We examined age in years (18–29, 30–39, 40–49, 50–59, and 60 years and older); mutually exclusive race/ethnicity (White, Black, Hispanic, Asian/Pacific Islander, American Indian/Alaska Native, another race or multiracial); sex-gender (cisgender man, cisgender woman, transgender man, transgender woman); CDC HIV transmission risk as collected on intake interviews with case management staff (heterosexual, injection drug use [IDU], transgender women and cisgender men who have sex with men [TW/MSM], TW/MSM who use injection drugs [TW/MSM/IDU], and other/unknown); CNICS site (Boston, MA, USA, Baltimore, MD, USA, San Diego, CA,

USA, Seattle, WA, USA); year of cohort entry (1995–2001, 2002–2007, 2008–2013, 2014–2018); cohort entry within the last year (no, yes); and number of site-specific GC/CT NAATs contributed over the entire follow-up period (continuous). Age was modeled as a time-varying covariate, while all other sociodemographic characteristics did not vary with time.

Table 1. Baseline Characteristics of People With HIV Engaged in Care, 4 US CNICS Sites, 2014–2018

Characteristic	n = 8455, No. (%)
Age	
16–29 y	859 (10.1)
30–39 y	1617 (19.1)
40–49 y	2482 (29.4)
50–59 y	2617 (31.0)
≥60 y	880 (10.4)
Race/ethnicity	
American Indian/Alaska Native	87 (1.0)
Asian/Pacific Islander	266 (3.1)
Black	2444 (28.9)
Hispanic	1537 (18.2)
White	3954 (46.8)
Another race, multiracial	167 (2.0)
Gender	
Cisgender man	6991 (82.7)
Cisgender woman	1355 (16.0)
Transgender man	5 (0.06)
Transgender woman	104 (1.2)
HIV transmission risk	
Heterosexual	1783 (21.1)
IDU	751 (8.9)
TW/MSM	4947 (58.5)
TW/MSM/IDU	630 (7.4)
Other/unknown	344 (4.1)
CNICS site	
Boston, MA	1334 (15.8)
Baltimore, MD	1899 (22.5)
San Diego, CA	2923 (34.6)
Seattle, WA	2299 (27.2)
Year of cohort entry	
1995–2001	1409 (16.7)
2002–2007	2071 (24.5)
2008–2013	2969 (35.1)
2014–2018	2006 (23.7)
Cohort entry in the last year	372 (4.4)
No. of follow-up intervals with a visit, median (IQR, range)	8 (6–11, 2–19)
No. of follow-up intervals with at least 1 GC/CT test, median (IQR, range)	
Any site	3 (1–5, 0–18)
Urogenital site	2 (1–4, 0–17)
Rectal site	0 (0–2, 0–16)
Pharyngeal site	0 (0–2, 0–17)
Any extragenital	0 (0–3, 0–17)
3-site	0 (0–1, 0–16)

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; IDU, injection drug use; IQR, interquartile range; TW/MSM, transgender women and cisgender men who have sex with men.

Time-Varying Clinical Characteristics

For testing analyses, we assessed whether GC/CT testing was more likely during intervals with concurrent syphilis and HCV enzyme-linked immunoassay (EIA) testing compared with intervals without this testing (ie, concurrent STI/HCV testing). As clinicians may change GC/CT testing practices based on clinical information from prior visits, we assessed the impact of a detectable HIV RNA (≥200 copies/mL), syphilis diagnosis, positive GC or CT NAAT at any anatomic site, and positive HCV EIA during 1 follow-up interval on GC/CT testing in the subsequent follow-up interval.

For incidence analyses, we assessed whether a GC/CT diagnosis at any anatomic site in 1 follow-up interval increased the risk of a site-specific infection in the subsequent interval. To assess the potential for enhanced HIV transmission in the context of a concurrent site-specific GC/CT infection, we examined whether GC/CT infections at a given anatomic site were more likely during an interval with a detectable viral load compared with intervals with an undetectable viral load. Finally, we assessed whether GC/CT infections at 1 anatomic site were more likely during intervals with GC/CT infections at another anatomic site (eg, GC/CT at both rectal and pharyngeal sites concurrently) and whether site-specific GC/CT infections were more likely during intervals with a concurrent syphilis diagnosis compared with those without a syphilis diagnosis.

We previously reported on the criteria used to assess syphilis diagnoses in a clinical cohort [11, 28].

Statistical Analysis

Using the concept of "time in coverage," we calculated the fraction of follow-up time covered by an annual GC/CT testing recommendation [29] by dividing the total follow-up time during which a participant had up-to-date GC/CT testing, defined as at least 1 test in a 12-month period, by the total follow-up time. We assessed the proportion of participants who had 100% time in coverage, meaning that they were tested for GC/CT at least yearly. The 12-month follow-up time was defined by participant follow-up time, not by calendar year.

Using survival analysis methods modified for recurrent events [30], we calculated site-specific GC/CT testing rates and site-specific GC, CT, and GC/CT incidence rates and 95% CIs overall and stratified by sociodemographic and clinical characteristics. For incidence calculations, the numerator included those with a positive GC or CT NAAT in their first follow-up interval, and the denominator included all participants, not just those tested for GC/CT.

Using Cox proportional hazards regression modified for recurrent events [30] and robust standard error estimation, we calculated crude and adjusted hazard ratios (aHRs) and 95% CIs comparing site-specific GC/CT testing and incidence rates by sociodemographic and clinical characteristics.

We included all variables of interest into multivariable testing models stratified by CNICS site and number of follow-up intervals with a visit to account for opportunities for GC/CT testing.

We ran 2 multivariable models for each incidence outcome of interest. The first included only sociodemographic characteristics, and the second included both sociodemographic and clinical characteristics. Multivariable models were adjusted for the total number of site-specific GC/CT tests contributed by each participant over the follow-up period (eg, the model of urogenital GC/CT incidence was adjusted for the total number of urogenital GC/CT tests a participant received during their follow-up time) and were stratified by CNICS site.

We defined statistical significance as $P < .05$. Log–log plots and comparisons of Kaplan-Meier-observed survival curves and Cox-predicted curves did not reveal violations of the proportional hazards assumption.

We computed the number needed to test (NNT) to detect a positive GC/CT NAAT. NNT was defined as the number of participants tested for GC/CT at a specific anatomic site divided by the number of participants with a positive GC/CT NAAT at that site in each calendar year of follow-up [31]. For participants with recurrent positive site-specific GC/CT NAATs in 1 year, we counted the first. We calculated annualized NNTs and 95% CIs overall and by sociodemographic characteristics. To estimate an upper bound of NNTs, we conducted a sensitivity analysis in which we recalculated NNTs assuming that those who were not tested in each calendar year would have had a negative GC/CT NAAT.

We used STATA 16.0 (StataCorp, College Station, TX, USA).

RESULTS

Study Population

During the study period, 8455 participants contributed 29 567.5 person-years of follow-up time (median [range], 4 [1–5] years). Ten percent of participants were aged 16–29 years (median [range], 47 [16–87] years), 28.9% were non-Hispanic Black, 18.1% were Hispanic (Table 1). Sixteen percent were cisgender women, and 1.2% were transgender women. TW/MSM comprised 58.5% of the sample, and 4.4% entered the cohort in the prior year.

Anatomic Site–Specific Testing

Of 8455 PWH, 2460 (29.1%) and 1123 (13.3%) had testing at any site and extragenital sites, respectively, at least yearly during follow-up. Of 5577 TW/MSM, 1961 (35.2%) and 1065 (19.1%) had testing at any site and extragenital sites, respectively, at least yearly during follow-up. Of the 37 cisgender women <25 years of age, 19 (51.3%) were screened at any site at least yearly during follow-up. Over the follow-up period, 1429 (16.9%) participants were never screened for GC/CT at any site; 1686 (19.9%), 4817 (57.0%), and 4791 (56.7%) were never screened at the urogenital, rectal, and pharyngeal sites, respectively.

There were 24 894 urogenital NAATs for a rate of 84 urogenital tests per 100 person-years (95% CI, 83–85), 12 286 rectal NAATs for a rate of 41 rectal tests per 100 person-years (95% CI, 41–42), and 11 658 pharyngeal tests for a rate of 39 pharyngeal tests per 100 person-years (95% CI, 39–40) (Table 2).

Rates of GC/CT testing at all sites were higher among PWH 16–39 years old compared with PWH 40–49 years old, among TW/MSM and TW/MSM/IDU compared with heterosexuals, and among PWH who entered the cohort more recently compared with those who entered the cohort from 1995 to 2001 (Table 3). Rates of urogenital testing were greater among Black and Hispanic PWH compared with White PWH and among cisgender women compared with cisgender men. Compared with cisgender men, rates of rectal and pharyngeal testing were lower among cisgender women but greater among transgender women. Rates of rectal testing were lower among Black PWH compared with White PWH.

Rates of testing at all sites were greater during intervals in which PWH were tested for syphilis and after intervals with a positive GC or CT NAAT or a syphilis diagnosis. Rates of rectal and pharyngeal, but not urogenital, testing were greater after intervals with a positive HCV EIA. In contrast, rates of testing at all sites were lower after intervals in which participants had a detectable HIV RNA compared with after intervals in which PWH had an undetectable HIV RNA.

Anatomic Site-Specific GC Infections

There were 503 urogenital, 960 rectal, and 805 pharyngeal GC infections, for rates of 1.7 (95% CI, 1.6–1.9), 3.2 (95% CI, 3.0–3.5), and 2.7 (95% CI, 2.5–2.9) infections per 100 person-years, respectively (Supplementary Table 1). Of the 8455 participants, 402 (4.7%) experienced 503 urogenital GC infections, of which 173 (34.4%) were recurrent; 651 (7.7%) participants experienced 960 rectal GC infections, of which 507 (52.8%) were recurrent; and 604 (7.1%) participants experienced 805 pharyngeal GC infections, of which 340 (42.2%) were recurrent. Of the 2268 GC infections, 336 (14.8%) were urogenital only, 632 (27.9%) were rectal only, 492 (21.7%) were pharyngeal only, 138 (6.1%) were urogenital and rectal, 108 (4.8%) were urogenital and pharyngeal, 430 (19.0%) were rectal and pharyngeal, and 132 (5.8%) were urogenital, rectal, and pharyngeal.

Anatomic Site–Specific CT Infections

There were 561 urogenital infections, 1258 rectal infections, and 266 pharyngeal CT infections, for rates of 1.9 (95% CI, 1.7–2.1), 4.3 (95% CI, 4.0–4.5), and 0.9 (95% CI, 0.8–1.0) infections per 100 person-years, respectively (Supplementary Table 1). Of the 8455 participants, 465 (5.5%) participants

Table 2. Rates of Site-Specific Gonorrhea and Chlamydia Testing by Sociodemographic and Time-Varying Clinical Characteristics Among People With HIV Engaged in Care, 4 US CNICS Sites, 2014–2018

		No. of GC/CT Tests (Rate per 100 Person-Years; 95% CI) by Anatomic Site				
	Person-Years	Urogenital	Rectal	Pharyngeal	Any Extragenital[a]	Any Site[b]
Overall	29 567.5	24 894 (84; 83–85)	12 286 (41; 41–42)	11 658 (39; 39–40)	14 694 (49; 49–50)	28 530 (96; 95–98)
Sociodemographic characteristics						
Age						
16–29 y	1924.75	2860 (149; 143–154)	1931 (100; 96–105)	1948 (101; 97–106)	2249 (117; 112–122)	3255 (169; 163–175)
30–39 y	5140.25	5872 (114; 111–117)	3676 (71; 69–74)	3534 (69; 66–71)	4264 (82; 80–85)	6722 (131; 128–134)
40–49 y	7757.75	6747 (87; 85–89)	3347 (43; 42–45)	3074 (40; 38–41)	3972 (51; 50–53)	7771 (100; 98–102)
50–59 y	10 327	7061 (68; 67–70)	2740 (26; 25–27)	2519 (24; 23–25)	3391 (33; 32–34)	8137 (79; 77–80)
≥60 y	4417.75	2354 (53; 51–55)	574 (13; 12–14)	583 (13; 12–14)	773 (17; 16–19)	2645 (60; 58–62)
Race/ethnicity						
American Indian/Alaska Native	300.5	246 (82; 72–93)	135 (45; 38–53)	147 (49; 42–57)	163 (54; 46–63)	279 (93; 83–104)
Asian/Pacific Islander	912.5	849 (93; 87–99)	564 (62; 57–67)	516 (57; 52–62)	634 (69; 54–75)	1003 (110; 103–117)
Black	8593	6089 (71; 69–73)	1733 (20; 19–21)	1845 (21; 20–22)	2184 (25; 24–26)	6782 (79; 77–81)
Hispanic	5407.25	6021 (111; 109–114)	3189 (59; 57–61)	3078 (57; 55–59)	3765 (70; 67–72)	6837 (126; 123–129)
White	13 820.75	11 119 (80; 79–82)	6357 (46; 45–47)	5805 (42; 41–43)	7576 (55; 54–56)	12 979 (94; 92–95)
Another race, multiracial	533.5	570 (107; 98–116)	290 (54; 48–61)	264 (49; 44–56)	327 (61; 55–68)	650 (122; 113–132)
Gender						
Cisgender man	24 422	21 310 (87; 86–88)	11 906 (49; 48–50)	11 202 (46; 45–47)	14 118 (58; 57–59)	24 693 (101; 100–102)
Cisgender woman	4767.75	3203 (67; 65–69)	112 (2; 2–3)	198 (4; 4–5)	241 (5; 4–6)	3388 (71; 69–73)
Transgender man	17.5	23 (131; 87–198)	8 (46; 23–91)	8 (46; 23–91)	9 (51; 27–99)	23 (131; 87–198)
Transgender woman	360.25	358 (99; 90–110)	242 (67; 59–76)	250 (69; 61–78)	281 (78; 69–88)	426 (118; 107–130)
HIV transmission risk						
Heterosexual	6244	3950 (63; 61–65)	282 (5; 4–5)	371 (6; 5–7)	477 (8; 7–8)	4257 (68; 66–70)
IDU	2618.25	1420 (54; 51–57)	104 (4; 3–5)	145 (6; 5–7)	169 (6; 5–7)	1503 (57; 54–60)
TW/MSM	17 433	16 842 (97; 95–98)	10 395 (60; 58–61)	9641 (55; 45–56)	12 246 (70; 69–71)	19 672 (113; 111–114)
TW/MSM/IDU	2167.5	1789 (82; 79–86)	1243 (57; 54–60)	1271 (59; 55–62)	1463 (67; 64–71)	2123 (98; 94–102)
Other/unknown	1104.75	893 (81; 76–86)	244 (22; 19–25)	230 (21; 18–24)	294 (27; 24–30)	975 (88; 83–94)
Year of cohort entry						
1995–2001	5294.75	3142 (59; 57–61)	993 (19; 18–20)	954 (18; 17–19)	1255 (24; 22–25)	3607 (68; 66–70)
2002–2007	7805.75	5774 (74; 72–76)	2497 (32; 31–33)	2270 (29; 28–30)	3006 (38; 37–40)	6652 (85; 83–87)
2008–2013	10 946.5	9749 (89; 87–91)	4907 (45; 43–46)	4616 (42; 41–43)	5865 (53; 52–55)	11 111 (101; 100–103)
2014–2018	5520.5	6229 (113; 110–116)	3871 (70; 68–72)	3818 (69; 67–71)	4523 (82; 80–84)	7160 (130; 127–133)
Time-varying clinical characteristics						
Syphilis testing, current interval						
No	14 104.75	4790 (34; 33–35)	2451 (17; 17–18)	1994 (14; 13–15)	3043 (22; 21–22)	6672 (47; 46–48)
Yes	15 462.75	20 104 (130; 128–132)	9817 (63; 62–65)	9664 (62; 61–64)	11 606 (75; 74–76)	21 858 (141; 139–143)
HCV EIA, current interval						
No	23 278.5	17 284 (74; 73–75)	866 (37; 36–38)	8227 (35; 34–36)	10 458 (45; 44–46)	20 328 (87; 86–88)
Yes	6289	7610 (121; 118–124)	3605 (57; 55–59)	3431 (54; 53–56)	4194 (67; 65–69)	8202 (130; 128–133)
Detectable HIV RNA, prior interval[c]						
No	24 346.5	19 183 (79; 78–80)	9717 (40; 39–41)	9183 (38; 37–38)	11 603 (48; 47–49)	22 058 (91; 89–92)
Yes	3107.25	2270 (73; 70–76)	1024 (33; 31–35)	1046 (34; 32–36)	1248 (40; 38–42)	2614 (84; 81–87)
Any site GC NAAT positive, prior interval[c]						
No	26 806.5	20 287 (76; 75–77)	9764 (36; 36–37)	9295 (35; 34–35)	11 762 (44; 43–45)	23 351 (87; 86–88)
Yes	647.25	1166 (180; 170–191)	977 (151; 142–161)	934 (144; 135–154)	1089 (168; 158–178)	1321 (204; 193–215)
Any site CT NAAT positive, prior interval[c]						
No	26 763.75	20 266 (76; 74–77)	9693 (36; 35–37)	9275 (35; 34–35)	11 705 (44; 43–44)	23 305 (87; 86–88)
Yes	690	1187 (172; 162–182)	1048 (152; 143–161)	954 (138; 130–147)	1146 (166; 157–176)	1367 (198; 188–209)
Incident syphilis, prior interval[c]						
No	26 914.25	20 771 (77; 76–78)	10 228 (38; 37–39)	9751 (36; 35–37)	12 262 (46; 45–46)	23 872 (89; 88–90)

Table 2. Continued

		No. of GC/CT Tests (Rate per 100 Person-Years; 95% CI) by Anatomic Site				
	Person-Years	Urogenital	Rectal	Pharyngeal	Any Extragenital[a]	Any Site[b]
Yes	539.5	682 (126; 117–136)	513 (95; 87–104)	478 (89; 81–97)	589 (109; 101–118)	800 (148; 138–159)
Positive HCV EIA, prior interval[c]						
No	27 148	21 236 (78; 77–79)	10 609 (39; 38–40)	10 098 (37; 36–38)	12 689 (47; 46–48)	24 409 (90; 89–91)
Yes	305.75	217 (71; 62–81)	132 (43; 36–51)	131 (43; 36–51)	162 (53; 45–62)	263 (86; 76–97)

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; EIA, enzyme-linked immunoassay; GC, gonorrhea; HCV, hepatitis C virus; IDU, injection drug use; NAAT, nucleic acid amplification test; TW/MSM, transgender women and cisgender men who have sex with men.

[a]Includes testing at either the rectal or pharyngeal site or both.

[b]Includes 541 (1.9%) tests at unspecified sites.

[c]Follow-up time for indicated time-varying covariates was 27 453.75 person-years as there was no interval before the first follow-up interval.

experienced 561 urogenital CT infections, of which 172 (30.7%) were recurrent; 855 (10.1%) experienced 1258 rectal CT infections, of which 672 (53.4%) were recurrent; and 224 (2.6%) participants experienced 266 pharyngeal CT infections, of which 61 (22.9%) were recurrent. Of the 2085 CT infections, 458 (22.0%) were urogenital only, 1116 (53.5%) were rectal only, 183 (8.8%) were pharyngeal only, 154 (7.4%) were urogenital and rectal, 36 (1.7%) were urogenital and pharyngeal, 114 (5.5%) were rectal and pharyngeal, and 24 (1.1%) were urogenital, rectal, and pharyngeal.

Correlates of Anatomic Site–Specific GC/CT Infections

There were 968 urogenital, 1915 rectal, and 1021 pharyngeal GC/CT infections, for rates of 3.3 (95% CI, 3.1–3.5), 6.5 (95% CI, 6.2–6.8), and 3.4 (95% CI, 3.2–3.7) infections per 100 person-years (Table 4). Compared with PWH age 40–49 years, the rates of GC/CT at all sites were greater among PWH age 16–39 years and lower among PWH age 50 years and older (Table 5). Compared with White PWH, the rate of urogenital GC was lower among Asian/Pacific Islander and Hispanic PWH and greater among Black PWH. In contrast, the rates of extragenital GC/CT were lower among Black PWH compared with White PWH. Cisgender women experienced lower rates of rectal and pharyngeal GC compared with cisgender men. Compared with heterosexuals, TW/MSM and TW/MSM/IDU experienced greater rates of GC/CT at all sites. The rates of extragenital GC/CT were greater among those who entered the CNICS cohort within the prior year compared with those who entered the cohort earlier.

In models adjusted for sociodemographic covariates, rates of GC/CT at all sites were greater during intervals after a positive GC/CT NAAT at any anatomic site compared with intervals after a negative GC/CT NAAT (Table 6). Rates of GC/CT at all sites were greater during intervals in which PWH had a positive GC/CT NAAT at another anatomic site compared with intervals without a positive GC/CT NAAT at other anatomic sites. Rates of extragenital GC/CT were greater during intervals in which PWH were also diagnosed with syphilis compared with intervals without a syphilis diagnosis. The rates of urogenital GC/CT, but not extragenital GC/CT, were greater during intervals in which PWH had a detectable viral load compared with intervals in which PWH had an undetectable viral load. This association was statistically significant among TW/MSM (aHR, 1.26; 95% CI, 1.01–1.43), but not among cisgender women (aHR, 1.24; 95% CI, 0.59–2.59) or heterosexual cisgender men (aHR, 1.68; 95% CI, 0.75–3.78).

Anatomic Site–Specific Number Needed to Test

The numbers of PWH needed to test (NNT) to detect 1 GC/CT infection at urogenital, rectal, and pharyngeal sites were 20 (95% CI, 19–21), 5 (95% CI, 5–5), and 9 (95% CI, 8–9), respectively (Table 7). NNTs for extragenital GC/CT were lower than for urogenital GC/CT across all sociodemographic groups. NNTs for all anatomic sites were lowest in PWH 16–29 years of age and increased with age.

In sensitivity analyses, NNTs at all anatomic sites in PWH 16–39 years of age remained low. NNTs for rectal GC/CT remained low in cisgender men and transgender women, in TW/MSM and TW/MSM/IDU, and in all racial and ethnic groups except Black PWH. While NNTs at extragenital sites were lower than NNTs at the urogenital site for cisgender women, heterosexuals, and PWID based on the number of participants screened, NNTs for the urogenital site were lower in these groups in the sensitivity analysis.

DISCUSSION

Among PWH participating in a clinical cohort at 4 clinical sites across the United States, only one-third were tested at least annually for GC/CT at any site. TW/MSM, who experience rectal and pharyngeal infections at a greater rate than urogenital infections [7], had a rate of extragenital testing almost 30% lower than that of urogenital testing (70 extragenital tests per 100 person-years vs 97 urogenital tests per 100 person-years).

GC/CT infections may increase the risk of onward HIV transmission [10]. However, our data indicate that the rate of GC/CT testing at any site was lower after intervals in which PWH had a detectable viral load. Clinic visits in which PWH have a detectable viral load may typically focus on restarting antiretroviral therapy, adherence support, and case management

Table 3. Bivariable and Multivariable Models of Site-Specific Gonorrhea and Chlamydia Testing and Sociodemographic and Time-Varying Clinical Covariates Among People With HIV Engaged in Care, 4 US CNICS Sites, 2014–2018

	Urogenital				Rectal				Pharyngeal			
	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value
Age												
16–29 y	1.70 (1.61–1.80)	<.001	1.32 (1.25–1.38)	<.001	2.36 (2.14–2.59)	<.001	1.54 (1.42–1.67)	<.001	2.60 (2.36–2.86)	<.001	1.61 (1.48–1.76)	<.001
30–39 y	1.32 (1.26–1.38)	<.001	1.15 (1.11–1.19)	<.001	1.66 (1.53–1.80)	<.001	1.30 (1.22–1.39)	<.001	1.74 (1.60–1.89)	<.001	1.35 (1.26–1.44)	<.001
40–49 y	Ref		Ref		Ref		Ref		Ref		Ref	
50–59 y	0.78 (0.75–0.82)	<.001	0.85 (0.82–0.88)	<.001	0.61 (0.55–0.66)	<.001	0.69 (0.64–0.75)	<.001	0.60 (0.55–0.66)	<.001	0.70 (0.65–0.76)	<.001
≥60 y	0.61 (0.57–0.65)	<.001	0.72 (0.68–0.76)	<.001	0.29 (0.25–0.34)	<.001	0.40 (0.34–0.46)	<.001	0.32 (0.27–0.38)	<.001	0.44 (0.38–0.52)	<.001
Race/ethnicity												
American Indian/Alaska Native	1.02 (0.82–1.26)	.005	0.97 (0.82–1.15)	.771	0.98 (0.67–1.43)	.914	0.91 (0.70–1.69)	.452	1.17 (0.82–1.66)	.387	0.95 (0.76–1.17)	.613
Asian/Pacific Islander	1.16 (1.04–1.29)	.858	0.98 (0.91–1.06)	.670	1.35 (1.15–1.59)	<.001	1.03 (0.91–1.17)	.637	1.35 (1.14–1.61)	.001	0.98 (0.85–1.13)	.788
Black	0.89 (0.84–0.93)	<.001	1.06 (1.01–1.11)	.011	0.44 (0.39–0.49)	<.001	0.88 (0.81–0.96)	.004	0.51 (0.46–0.57)	<.001	0.95 (0.88–1.04)	.267
Hispanic	1.38 (1.32–1.45)	<.001	1.06 (1.02–1.10)	.001	1.28 (1.18–1.39)	<.001	0.97 (0.91–1.04)	.389	1.35 (1.24–1.47)	<.001	1.00 (0.94–1.07)	.909
White	Ref		Ref		Ref		Ref		Ref		Ref	
Another race, multiracial	1.32 (1.17–1.49)	<.001	1.01 (0.92–1.11)	.841	1.18 (0.95–1.46)	.136	0.85 (0.69–1.04)	.115	1.17 (0.95–1.45)	.143	0.90 (0.73–1.10)	.294
Gender												
Cisgender man	Ref		Ref		Ref		Ref		Ref		Ref	
Cisgender woman	0.77 (0.74–0.81)	<.001	1.24 (1.17–1.31)	<.001	0.05 (0.04–0.06)	<.001	0.27 (0.20–0.37)	<.001	0.09 (0.07–0.11)	<.001	0.43 (0.33–0.56)	<.001
Transgender man	1.52 (1.02–2.25)	.038	1.36 (0.85–2.18)	.198	0.94 (0.17–5.32)	.949	1.04 (0.23–4.60)	.960	1.01 (0.18–5.68)	.994	1.72 (0.31–9.40)	.534
Transgender woman	1.13 (0.96–1.33)	.134	1.03 (0.91–1.16)	.657	1.37 (1.10–1.69)	.004	1.17 (1.00–1.38)	.053	1.49 (1.20–1.86)	<.001	1.26 (1.05–1.51)	.012
HIV transmission risk												
Heterosexual	Ref		Ref		Ref		Ref		Ref		Ref	
IDU	0.86 (0.79–0.93)	<.001	0.99 (0.93–1.07)	.916	0.88 (0.61–1.27)	.492	0.89 (0.61–1.30)	.542	0.93 (0.68–1.27)	.655	1.06 (0.77–1.45)	.724
TW/MSM	1.51 (1.44–1.59)	<.001	1.22 (1.15–1.28)	<.001	13.1 (10.7–16.1)	<.001	5.61 (3.65–5.83)	<.001	9.20 (7.71–11.0)	<.001	3.99 (3.24–4.91)	<.001
TW/MSM/IDU	1.30 (1.20–1.42)	<.001	1.22 (1.13–1.31)	<.001	12.7 (10.1–15.9)	<.001	4.47 (3.50–5.72)	<.001	9.87 (8.08–12.0)	<.001	3.84 (3.08–4.79)	<.001
Other/unknown	1.27 (1.14–1.41)	<.001	1.04 (0.96–1.13)	.309	4.86 (3.46–6.84)	<.001	2.72 (1.99–3.72)	<.001	3.48 (2.55–4.74)	<.001	2.26 (1.72–2.98)	<.001
Year of cohort entry												
1995–2001	Ref		Ref		Ref		Ref		Ref		Ref	
2002–2007	1.24 (1.16–1.33	<.001	1.07 (1.02–1.13)	.010	1.70 (1.47–1.97)	<.001	1.25 (1.10–1.42)	<.001	1.61 (1.38–1.87)	<.001	1.21 (1.07–1.38)	.003
2008–2013	1.50 (1.40–1.59)	<.001	1.11 (1.06–1.17)	<.001	2.38 (2.07–2.73)	<.001	1.33 (1.18–1.50)	<.001	2.33 (2.03–2.68)	<.001	1.33 (1.18–1.50)	<.001
2014–2018	1.91 (1.80–2.04)	<.001	1.36 (1.29–1.44)	<.001	3.83 (3.34–4.39)	<.001	1.86 (1.64–2.11)	<.001	3.97 (3.46–4.55)	<.001	1.89 (1.67–2.14)	<.001
Syphilis testing, current interval												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	3.78 (3.64–3.92)	<.001	3.23 (3.11–3.36)	<.001	3.61 (3.42–3.81)	<.001	2.09 (1.98–2.21)	<.001	4.37 (4.14–4.62)	<.001	2.63 (2.48–2.78)	<.001
HCV EIA, current interval												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.56 (1.52–1.60)	<.001	1.00 (0.98–1.03)	.804	1.49 (1.43–1.56)	<.001	0.93 (0.89–0.97)	<.001	1.50 (1.43–1.56)	<.001	0.94 (0.90–0.98)	.003
Detectable HIV RNA, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	0.86 (0.92–1.01)	.094	0.96 (0.92–0.99)	.029	0.85 (0.78–0.93)	<.001	0.89 (0.83–0.96)	.001	0.93 (0.85–1.01)	.077	0.91 (0.85–0.98)	.010

Table 3. Continued

	Urogenital				Rectal				Pharyngeal			
	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value
Any site GC NAAT positive, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	2.36 (2.25–2.49)	<.001	1.33 (1.26–1.39)	<.001	4.11 (3.85–4.39)	<.001	1.47 (1.38–1.57)	<.001	4.11 (3.84–4.40)	<.001	1.45 (1.36–1.56)	<.001
Any site CT NAAT positive, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	2.28 (2.17–2.40)	<.001	1.33 (1.26–1.40)	<.001	4.21 (3.95–4.48)	<.001	1.68 (1.58–1.79)	<.001	4.01 (3.75–4.28)	<.001	1.58 (1.48–1.69)	<.001
Syphilis diagnosis, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.63 (1.52–1.74)	<.001	1.03 (0.97–1.10)	.381	2.48 (2.28–2.70)	<.001	1.19 (1.10–1.29)	<.001	2.42 (2.21–2.65)	<.001	1.19 (1.09–1.29)	<.001
Positive HCV EIA, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	0.93 (0.82–1.06)	.259	0.96 (0.86–1.08)	.494	1.13 (0.94–1.34)	.187	1.20 (1.02–1.41)	.029	1.18 (0.98–1.41)	.072	1.24 (1.05–1.46)	.010

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; EIA, enzyme-linked immunoassay; GC, gonorrhea; HCV, hepatitis C virus; IDU, injection drug use; NAAT, nucleic acid amplification test; TW/MSM, transgender women and cisgender men who have sex with men.

[a]Multivariable model stratified by CNICS site and total number of intervals with a visit contributed by each participant.

[b]Total follow-up time for indicated bivariable models and all multivariable models was 27 453.75 person-years due to time-varying covariates.

to address viral suppression rather than STI testing. However, STI testing may also need to be prioritized during these visits to reduce the risk of HIV and STI transmission to sexual partners.

Self-testing is a feasible, acceptable, and effective strategy to increase extragenital screening among PWH [27]. Nursing-initiated self-testing before a provider visit, visual prompts to providers to collect extragenital specimens, and bundled electronic medical record order sets that include extragenital self-testing as part of routine labs may facilitate routine GC/CT testing [32]. In addition, clinical reminders, provider performance feedback on GC/CT testing, and equity in reimbursement for cognitive services relative to procedural services may further increase STI testing.

Lower testing rates may reflect concern about experiencing stigma or discrimination when disclosing sexual behavior to providers, particularly receptive anal sex. These data underscore the importance of provider training to ensure that clinicians actively inquire about their patients' sexual behavior, offer appropriate testing modalities, and create a supportive environment in which PWH are comfortable disclosing their sexual behaviors so that they receive appropriate testing and counseling. Many resources are available to facilitate such training (eg, www.lgbtqiahealth.org).

The rates of GC and CT, particularly rates of extragenital infections, are high and consistent with increasing incidence documented in other clinical cohorts of PWH [3, 5, 6]. Greater than 70% of all GC and CT infections among PWH were extragenital, and >50% of rectal GC and CT infections were recurrent. Almost 70% of GC infections were at rectal, pharyngeal, or concurrent rectal and pharyngeal sites, and >50% of CT infections were at the rectal site only. Consistent with prior studies, younger PWH experienced greater rates of GC/CT at each anatomic site, while TW/MSM experienced greater rates of extragenital GC/CT [3, 5, 6, 33]. Black PWH were more likely to experience urogenital CT infections compared with White PWH.

Rates of GC/CT infections at 1 anatomic site were greater during intervals in which PWH had a GC/CT infection at another site. Thus, increasing extragenital testing, particularly rectal testing, may be an efficient way to reduce population-level GC/CT incidence among MSM [34]. Extragenital GC/CT infections were more common during intervals in which PWH were also diagnosed with syphilis. Therefore, routine multisite testing for GC/CT, especially at extragenital sites, should be integrated with syphilis testing. Mucosal inflammation caused by GC/CT infection may facilitate *Treponema pallidum* infection, and, conversely, extragenital chancres, which are often missed on clinical exam, may facilitate GC/CT infection of the rectal and pharyngeal mucosa. As we do not know the timing of *Treponema pallidum* infection in relation to GC/CT infection, we cannot draw conclusions about the directionality of this association.

Table 4. Rates of Site-Specific Gonorrhea and Chlamydia Incidence by Sociodemographic and Time-Varying Clinical Characteristics, 4 US CNICS Sites, 2014–2018

		No. of Incident GC/CT Infections (Rate per 100 Person-Years; 95% CI)		
	Person-Years	Urogenital	Rectal	Pharyngeal
Overall	29 567.5	968 (3.3; 3.1–3.5)	1915 (6.5; 6.2–6.8)	1021 (3.4; 3.2–3.7)
Age				
16–29 y	1924.75	196 (10.2; 8.8–11.7)	465 (24.2; 22.1–26.5)	262 (13.6; 12.1–15.4)
30–39 y	5140.25	293 (5.7; 5.1–6.4)	652 (12.7; 11.7–13.7)	352 (6.8; 6.2–7.6)
40–49 y	7757.75	272 (3.5; 3.1–3.9)	486 (6.3; 5.7–6.8)	264 (3.4; 3.0–3.8)
50–59 y	10 327	174 (1.7; 1.4–1.9)	271 (2.6; 2.3–3.0)	120 (1.2; 1.0–1.4)
≥60 y	4417.75	33 (0.7; 0.5–1.0)	41 (0.9; 0.7–1.3)	23 (0.5; 0.3–0.8)
Race/ethnicity				
American Indian/Alaska Native	300.5	14 (4.7; 2.8–7.9)	26 (8.7; 5.9–12.7)	19 (6.3; 4.0–9.9)
Asian/Pacific Islander	912.5	26 (2.8; 1.9–4.2)	93 (10.2; 8.3–12.5)	46 (5.0; 3.8–6.7)
Black	8593	217 (2.5; 2.2–2.9)	245 (2.8; 2.5–3.2)	152 (1.8; 1.5 2.1)
Hispanic	5407.25	212 (3.9; 3.4–4.5)	508 (9.4; 8.6–10.2)	293 (5.4; 4.8–6.1)
White	13 820.75	471 (3.4; 3.1–3.7)	988 (7.1; 6.7–7.6)	485 (3.5; 3.2–3.8)
Another race, multiracial	533.5	28 (5.2; 3.6–7.6)	55 (10.3; 7.9–13.4)	26 (4.9; 3.3–7.2)
Gender				
Cisgender man	24 422	913 (3.7; 3.5–4.0)	1882 (7.7; 7.4–8.1)	1002 (4.1; 3.9–4.4)
Cisgender woman	4767.75	45 (0.9; 0.7–1.3)	4 (0.1; 0.03–0.2)	8 (0.2; 0.1–0.3)
Transgender man	17.5	2 (11.4; 2.8–45)	1 (5.7; 0.8–40.6)	0
Transgender woman	360.25	8 (2.2; 1.1–4.4)	28 (7.8; 5.4–11.3)	11 (3.0; 1.7–5.5)
HIV transmission risk				
Heterosexual	6244	63 (1.0; 0.7–1.3)	19 (0.3; 0.2–0.5)	24 (0.4; 0.3–0.6)
IDU	2618.25	14 (0.5; 0.3–0.9)	9 (0.3; 0.2–0.7)	2 (0.1; 0.02–0.3)
TW/MSM	17 433	781 (4.5; 4.2–4.8)	1669 (9.6; 9.1–10.0)	858 (4.9; 4.6–5.3)
TW/MSM/IDU	2167.5	95 (4.4; 3.6–5.4)	188 (8.7; 7.5–10.0)	119 (5.5; 4.6–6.6)
Other/unknown	1104.75	15 (1.4; 0.8–2.2)	30 (2.7; 1.9–3.9)	18 (1.6; 1.0–2.6)
Cohort entry within the prior year				
No	28 850	925 (3.2; 3.0–3.4)	1795 (6.2; 5.9–6.5)	959 (3.3; 3.1–3.5)
Yes	717.5	43 (6.0; 4.4–8.1)	120 (16.7; 14.0–20.0)	62 (8.6; 6.7–11.1)
Any site GC/CT NAAT positive, prior interval[a]				
No	24 585.5	693 (2.8; 2.6–3.0)	1292 (5.2; 5.0–5.5)	691 (2.8; 2.6–3.0)
Yes	1098.25	163 (14.8; 12.7–17.3)	385 (35.1; 31.7–38.7)	204 (18.6; 16.2–21.3)
Detectable HIV RNA, current interval				
No	25 942	826 (3.2; 3.0–3.4)	1670 (6.4; 6.1–6.7)	877 (3.4; 3.2–3.6)
Yes	3625.5	142 (3.9; 3.3–4.6)	245 (6.8; 5.9–7.7)	144 (4.0; 3.4–4.7)
Urogenital GC/CT NAAT positive, current interval				
No	29 169		1684 (5.8; 5.5–6.1)	863 (3.0; 2.8–3.2)
Yes	398.5		231 (58.0; 50.9–65.9)	158 (39.6; 33.9–46.3)
Rectal GC/CT NAAT positive, current interval				
No	28 793.5	737 (2.6; 2.4–2.7)		640 (2.2; 2.1–2.4)
Yes	774	231 (30.0; 26.2–33.9)		381 (49.2; 44.5–54.4)
Pharyngeal GC/CT NAAT positive, current interval				
No	29 158.25	810 (2.8; 2.6–3.0)	1534 (5.3; 5.0–5.5)	
Yes	409.25	158 (38.6; 33.0–45.1)	381 (93.1; 84.2–102)	
Syphilis diagnosis, current interval				
No	28 969.75	904 (3.1; 2.9–3.3)	1766 (6.1; 5.8–6.4)	940 (3.2; 3.0–3.5)
Yes	597.75	64 (10.7; 8.4–13.7)	149 (24.9; 21.2–29.3)	81 (13.6; 10.9–16.8)

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; GC, gonorrhea; IDU, injection drug use; NAAT, nucleic acid amplification test; TW/MSM, transgender women and cisgender men who have sex with men.

[a]Follow-up time for indicated time-varying covariate was 27 453.75 person-years as there was no interval before the first follow-up interval.

Similar to prior work [35, 36], we did not find an association between rectal or pharyngeal GC/CT and detectable plasma HIV RNA. Instead, we observed an association between urogenital GC/CT and a detectable viral load, particularly among TW/MSM. This finding suggests that PWH who practice condomless insertive sex may be more likely to transmit

Table 5. Bivariable and Multivariable Models of Site-Specific Gonorrhea/Chlamydia Incidence and Sociodemographic Covariates Among People With HIV Engaged in Care, 4 US CNICS Sites, 2014–2018

	Urogenital GC/CT				Rectal GC/CT				Pharyngeal GC/CT			
	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value
Age												
16–29 y	2.97 (2.36–3.73)	<.001	1.58 (1.24–2.01)	.019	3.93 (3.28–4.71)	<.001	1.73 (1.45–2.06)	<.001	4.18 (3.33–5.23)	<.001	1.74 (1.39–2.17)	<.001
30–39 y	1.63 (1.33–1.99)	<.001	1.15 (0.95–1.40)	.156	2.03 (1.73–2.38)	<.001	1.29 (1.12–1.50)	<.001	2.02 (1.65–2.47)	<.001	1.30 (1.07–1.56)	.007
40–49 y	Ref		Ref		Ref		Ref		Ref		Ref	
50–59 y	0.47 (0.37–0.60)	<.001	0.60 (0.48–0.74)	<.001	0.41 (0.33–0.51)	<.001	0.58 (0.48–0.70)	<.001	0.33 (0.26–0.43)	<.001	0.47 (0.37–0.60)	<.001
≥60 y	0.21 (0.14–0.31)	<.001	0.33 (0.23–0.49)	<.001	0.14 (0.10–0.21)	<.001	0.30 (0.21–0.43)	<.001	0.14 (0.09–0.24)	<.001	0.30 (0.18–0.50)	<.001
Race/ethnicity												
American Indian/Alaska Native	1.37 (0.73–2.57)	.321	1.03 (0.57–1.85)	.928	1.21 (0.60–2.43)	.587	1.03 (0.58–1.84)	.907	1.80 (0.83–3.89)	.134	1.08 (0.66–1.80)	.745
Asian/Pacific Islander	0.84 (0.54–1.29)	.427	0.66 (0.44–0.97)	.034	1.43 (1.03–1.98)	.032	1.03 (0.78–1.37)	.830	1.44 (0.98–2.13)	.066	0.97 (0.70–1.35)	.877
Black	0.75 (0.60–0.92)	.006	1.26 (1.02–1.54)	.028	0.40 (0.32–0.50)	<.001	0.81 (0.67–0.97)	.020	0.50 (0.39–0.65)	<.001	0.79 (0.63–0.98)	.029
Hispanic	1.15 (0.93–1.41)	.199	0.79 (0.64–0.96)	.020	1.31 (1.12–1.53)	.001	0.92 (0.80–1.06)	.267	1.54 (1.27–1.87)	<.001	1.01 (0.85–1.22)	.868
White	Ref		Ref		Ref		Ref		Ref		Ref	
Another race, multiracial	1.54 (0.89–2.65)	.122	1.22 (0.72–2.09)	.460	1.44 (0.95–2.16)	.083	1.23 (0.93–1.63)	.148	1.40 (0.89–2.19)	.146	1.48 (0.94–2.32)	.089
Gender												
Cisgender man	Ref		Ref		Ref		Ref		Ref		Ref	
Cisgender woman	0.25 (0.18–0.35)	<.001	0.79 (0.49–1.28)	.346	0.01 (0.003–0.04)	<.001	0.13 (0.04–0.44)	.001	0.04 (0.01–0.11)	<.001	0.28 (0.11–0.76)	.013
Transgender man	3.08 (0.55–17.2)	.200	3.00 (0.77–11.7)	.114	0.74 (0.13–4.16)	.737	0.83 (0.44–1.59)	.580	No events		No events	
Transgender woman	0.59 (0.19–1.85)	.367	0.48 (0.15–1.52)	.212	1.01 (0.64–1.59)	.975	0.80 (0.53–1.20)	.275	0.74 (0.31–1.76)	.495	0.48 (0.21–1.13)	.095
HIV transmission risk												
Heterosexual	Ref		Ref		Ref		Ref		Ref		Ref	
IDU	0.53 (0.28–1.02)	.057	0.72 (0.37–1.39)	.326	1.13 (0.39–3.27)	.821	1.18 (0.45–3.12)	.724	0.20 (0.05–0.86)	.031	0.22 (0.05–0.95)	.042
TW/MSM	4.42 (3.30–5.91)	<.001	2.17 (1.40–3.35)	<.001	31.4 (17.6–55.9)	<.001	4.69 (2.91–7.59)	<.001	12.8 (7.77–21.0)	<.001	2.43 (1.52–3.91)	<.001
TW/MSM/IDU	4.34 (2.99–6.30)	<.001	2.16 (1.34–3.49)	.002	28.5 (15.5–52.3)	<.001	5.00 (3.02–8.30)	<.001	14.3 (8.28–24.6)	<.001	2.46 (1.47–4.12)	.001
Other/unknown	1.34 (0.76–2.36)	.308	0.82 (0.43–1.56)	.546	8.89 (3.88–20.4)	<.001	2.32 (1.19–4.54)	.014	4.24 (1.98–9.08)	<.001	1.56 (0.84–2.89)	.160
Cohort entry within the prior year												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.88 (1.30–2.72)	.001	1.37 (0.88–2.15)	.164	2.66 (2.13–3.33)	<.001	1.79 (1.31–2.45)	<.001	2.67 (1.97–3.62)	<.001	1.73 (1.19–2.52)	.004

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; EIA, enzyme-linked immunoassay; GC, gonorrhea; IDU, injection drug use; TW/MSM, transgender women and cisgender men who have sex with men.

[a]Multivariable model adjusted for total number of site-specific GC/CT tests contributed by each participant over the follow-up period and stratified by CNICS site. Total follow-up time for all models was 29 567.5 person-years.

Table 6. Bivariable and Multivariable Models of Site-Specific Gonorrhea/Chlamydia Incidence and Time-Varying Clinical Covariates Among People With HIV Engaged in Care, 4 US CNICS Sites, 2014–2018

	Urogenital GC/CT				Rectal GC/CT				Pharyngeal GC/CT			
	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value	Crude HR (95% CI)	*P* Value	Adjusted HR[a] (95% CI)	*P* Value
Any site GC/CT NAAT positive, prior interval[b]												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	5.25 (4.38–6.30)	<.001	1.34 (1.11 (1.63)	.003	6.66 (5.86–7.58)	<.001	1.35 (1.19–1.53)	<.001	6.64 (5.57–7.90)	<.001	1.22 (1.03–1.44)	.021
Detectable HIV RNA, current interval												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	1.18 (0.97–1.43)	.097	1.26 (1.04–1.53)	.020	0.99 (0.85–1.16)	.917	1.09 (0.94–1.27)	.247	1.15 (0.95–1.39)	.149	1.09 (0.86–1.37)	.476
Urogenital GC/CT NAAT positive, current interval												
No					Ref		Ref		Ref		Ref	
Yes					9.93 (8.64–11.4)	<.001	2.53 (2.14–3.00)	<.001	13.3 (11.2–15.7)	<.001	2.68 (2.16–3.33)	<.001
Rectal GC/CT NAAT positive, current interval												
No	Ref		Ref						Ref		Ref	
Yes	11.5 (9.92–13.5)	<.001	2.90 (2.36–3.58)	<.001					30.5 (26.7–35.0)	<.001	4.73 (4.02–5.58)	<.001
Pharyngeal GC/CT NAAT positive, current interval												
No	Ref		Ref		Ref		Ref					
Yes	14.5 (12.2–17.5)	<.001	2.68 (2.12–3.40)	<.001	18.3 (16.4–20.5)	<.001	3.72 (3.26–4.23)	<.001				
Syphilis diagnosis, current interval												
No	Ref		Ref		Ref		Ref		Ref		Ref	
Yes	3.39 (2.64–4.34)	<.001	1.17 (0.88–1.55)	.285	4.02 (3.42–4.74)	<.001	1.45 (1.21–1.73)	<.001	4.16 (3.31–5.22)	<.001	1.42 (1.09–1.85)	.008

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; GC, gonorrhea; NAAT, nucleic acid amplification test.

[a]Multivariable models were adjusted for sociodemographic covariates and total number of site-specific GC/CT tests contributed by each patient over the follow-up period and stratified by CNICS site.

[b]Total follow-up time for indicated bivariable models and all multivariable models was 27 453.75 person-years due to time-varying covariates.

Table 7. Annualized Number Needed to Test to Detect 1 Positive Gonorrhea/Chlamydia Nucleic Acid Amplification Test by Anatomic Site and Sociodemographic Characteristics, 4 US CNICS Sites, 2014–2018

	NNT Based on Participants who Were Screened						NNT Based on the Assumption That Participants who Were Not Screened Would Have Had a Negative GC/CT NAAT					
	Urogenital GC/CT		Rectal GC/CT		Pharyngeal GC/CT		Urogenital GC/CT		Rectal GC/CT		Pharyngeal GC/CT	
	Tested/ Pos	NNT (95% CI)	Tested/ Pos	NNT (95% CI)	Tested/ Pos	NNT (95% CI)	Tested/ Pos	NNT (95% CI)	Tested/Pos	NNT (95% CI)	Tested/ Pos	NNT (95% CI)
Overall	17 934/ 898	20 (19–21)	8406/1651	5 (5–5)	8054/929	9 (8–9)	34 094/ 898	38 (36–41)	34 094/ 1651	21 (20–22)	34 094/ 929	37 (34–39)
Age												
16–29 y	1767/180	10 (9–11)	1208/378	3 (3–3)	1225/232	5 (5–6)	2371/180	13 (11–15)	2371/378	6 (6–7)	2371/232	10 (9–12)
30–39 y	3886/267	15 (13–16)	2372/564	4 (4–5)	2307/322	7 (6–8)	5963/267	22 (20–25)	5963/564	11 (10–11)	5963/322	19 (17–21)
40–49 y	4917/253	19 (17–22)	2358/425	6 (5–6)	2198/239	9 (8–10)	8983/253	36 (31–40)	8983/425	21 (19–23)	8983/239	38 (33–43)
50–59 y	5443/166	33 (28–38)	2022/247	8 (7–9)	1873/115	16 (14–20)	11 756/ 166	71 (61–83)	11 756/247	48 (42–54)	11 756/ 115	102 (85–124)
≥60 y	1920/32	60 (43–88)	446/37	12 (9–17)	442/21	21 (14–34)	5021/32	157 (111–229)	5021/37	136 (99–193)	5021/21	239 (157–386)
Race/ethnicity												
American Indian/Alaska Native	169/12	14 (8–27)	85/21	4 (3–6)	93/15	6 (4–11)	345/12	29 (17–55)	345/21	16 (11–26)	345/15	23 (14–41)
Asian/Pacific Islander	604/24	25 (17–39)	383/77	5 (4–6)	358/41	9 (7–12)	1061/24	44 (30–69)	1061/77	14 (11–17)	1061/41	26 (19–36)
Black	4753/200	24 (21–27)	1234/211	6 (5–7)	1317/140	9 (8–11)	9950/200	50 (43–57)	9950/211	47 (41–54)	9950/140	71 (60–84)
Hispanic	4126/192	21 (19–25)	2106/411	5 (4–5)	2035/260	8 (7–9)	6205/192	32 (28–37)	6205/441	14 (14–15)	6205/260	24 (21–27)
White	7889/445	18 (11–24)	4393/851	5 (5–5)	4058/449	9 (8–10)	15 908/ 445	36 (33–39)	15 908/851	19 (18–20)	15 908/ 449	35 (32–39)
Another race, multiracial	393/25	16 (11–24)	205/50	4 (3–5)	193/24	8 (6–12)	625/25	25 (17–38)	625/50	13 (10–17)	625/24	26 (18–40)
Gender												
Cisgender man	15 099/ 845	18 (17–19)	8135/1619	5 (5–5)	7706/913	8 (8–9)	23 114/ 845	27 (26–29)	23 114/ 1619	14 (14–15)	23 114/ 913	25 (24–27)
Cisgender woman	2575/44	59 (44–80)	99/3	33 (12–159)	172/6	39 (13–77)	5542/44	126 (94–173)	5524/3	1847 (632–8961)	5542/6	924 (425–2516)
Transgender man	18/2	9 (3–73)	5/1	5 (1–198)	5/0	…	21/2	11 (3–85)	21/1	21 (4–830)	21/0	…
Transgender woman	242/7	35 (17–85)	167/28	6 (4–9)	171/10	17 (10–35)	417/7	60 (29–148)	417/28	15 (10–22)	417/10	42 (23–87)
HIV transmission risk												
Heterosexual	3270/62	53 (41–69)	234/18	13 (8–22)	313/20	16 (10–25)	7256/62	117 (91–153)	7256/18	403 (255–680)	7256/20	363 (235–594)
IDU	1211/13	93 (55–175)	85/8	11 (6–24)	121/2	61 (17–498)	3024/13	233 (136–437)	3024/8	378 (192–875)	3024/2	1512 (419–12 484)
TW/MSM	11 537/ 718	16 (15–17)	7057/1434	5 (5–5)	6583/782	8 (8–9)	20 005/ 718	28 (26–30)	20 005/ 1434	14 (13–15)	20 005/ 782	26 (24–27)
TW/MSM/IDU	1260/90	14 (11–17)	843/167	5 (4–6)	871/107	8 (7–10)	2508/90	28 (23–35)	2508/167	15 (13–18)	2508/107	23 (19–28)
Other/unknown	656/15	44 (27–78)	169/24	7 (5–11)	166/18	9 (6–15)	1301/15	87 (53–155)	1301/24	54 (37–84)	1301/18	72 (46–122)

Abbreviations: CNICS, CFAR Network of Integrated Clinical Systems; CT, chlamydia; GC, gonorrhea; IDU, injection drug use; NAAT, nucleic acid amplification test; pos, number of participants with a positive site-specific GC/CT NAAT; tested, number of participants tested with a site-specific GC/CT NAAT; TW/MSM, transgender women and cisgender men who have sex with men.

HIV in the setting of both STI-related genital inflammation and detectable plasma HIV RNA compared with those with a suppressed viral load. We also found that an incident syphilis diagnosis in PWH was strongly associated with detectable HIV RNA, raising concerns that urogenital GC/CT and syphilis could potentiate onward HIV transmission [11]. While mathematical modeling studies have assessed the contribution of GC/CT to HIV transmission [10], future modeling studies of HIV transmission should incorporate the effects of both site-specific GC/CT and syphilis.

Taken together, the rates of site-specific GC/CT infection, the findings from the multivariable analyses, and the NNT estimates indicate that GC/CT testing should be routine among certain PWH [31]. PWH 16–39 years old may benefit from routine testing at all sites; NNTs in the sensitivity analysis doubled between the 30–39 and 40–49 age groups, indicating a potential cutoff for testing recommendations among PWH. Rectal testing is likely to be beneficial in PWH of all races and ethnicities. Extragenital testing should be routine among TW/MSM, with the addition of urogenital testing in TW/MSM who practice insertive sex. In addition, our data suggest that transgender women may benefit from routine extragenital testing and transgender men may benefit from routine urogenital and rectal testing. PWH with prior GC/CT, a detectable viral load, and syphilis should also be prioritized for routine GC/CT testing at all sites, the urogenital site, and extragenital sites, respectively. PWH who entered the CNICS cohort within the prior year, a proxy for recent care entry, may also benefit from routine extragenital testing. Furthermore, detection of extragenital GC/CT is critical to facilitating appropriate treatment and follow-up of site-specific infections and to thwarting further onward GC/CT transmission and antimicrobial resistance [13–21].

Cisgender women had greater rates of urogenital GC/CT infections compared with extragenital infections. However, the NNT for rectal infections among cisgender women was lower than the NNT for urogenital infections. Among cisgender women, rectal GC/CT testing may be more likely to be based on a participant's report of receptive anal sex rather than as part of routine testing; therefore, there is higher pretest probability of infection at the rectal site for each test performed. Among women with extragenital exposures, the prevalence of rectal CT was greater than urogenital CT [8]. In contrast, urogenital testing is more likely to be routine and urogenital exposure is more common leading to a greater incidence of urogenital infection but a greater NNT. Optimal prioritization and frequency of extragenital testing among cisgender women with HIV deserves further study [37], and before the 2021 revision of the CDC STI Treatment Guidelines, extragenital testing was not recommended in clinical guidelines [1].

Relatedly, we were not able to assess the reason for testing for study participants, whether routine testing regardless of risk group membership or exposures; routine testing based on risk-group membership (eg, youth, transgender women, MSM); testing based on site-specific exposures (eg, receptive anal sex); testing based on exposure to a partner with GC/CT or symptoms of GC/CT. We observed larger differences in NNTs based on the number screened and NNTs in the sensitivity analysis among some groups of PWH (eg, older PWH, cisgender women, PWID, heterosexuals) compared with others (youth, TW/MSM, TW/MSM/IDU) whose testing is more likely to be exposure-based rather than routine based on risk-group membership.

This work has important limitations. Not all syphilis testing and diagnosis occurs within the context of HIV care. For example, Baltimore, San Diego, and Seattle have robust local public health sexual health clinics where patients participating in those CNICS sites may access STI testing. As GC/CT infections diagnosed outside HIV care are not necessarily captured in CNICS data, our data likely underestimate rates of GC/CT infections. We did not include behavioral data, including sexual practices and substance use, in our analyses. We have likely included participants who are not sexually active which would lead to underestimation of the incidence of GC/CT in these analyses. Future studies should include behavioral data to better direct testing and prevention resources to those who need them most. Finally, our data may not be generalizable to PWH receiving care in other geographic areas.

Routine testing for site-specific GC/CT infections among PWH should be prioritized as a critical component of HIV care, particularly among younger PWH, TW/MSM, and PWH with prior GC/CT infections, a detectable viral load, and syphilis.

Supplementary Data

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

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