Neisseria gonorrhea incidence and testing in the HIV Outpatient Study, 2007-2017

#1168

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BACKGROUND

- **Co-infection with *Neisseria gonorrhea* (GC) increases HIV transmission to uninfected partners.**
- **Since 2013, incidence of GC has been increasing in the United States (US).**

OBJECTIVES

- **We assessed temporal trends in incidence and testing rates, and associated risk factors of incident GC among people living with HIV (PLWH).**
- **We also examined the status of up-to-date GC testing and anatomic testing sites, and identified correlates of GC testing among HIV-positive men who have sex with men (MSM).**

METHODS

- **We analyzed medical records data from HIV Outpatient Study (HOPS) cohort participants who received HIV care at nine US HIV clinics during 1/1/2007 to 9/30/2017.**
- **Incident GC cases were defined based on laboratory results, clinical diagnoses, and treatments.**
- **We assessed the trends in GC incidence and testing rates from 2007-2017 among HIV-positive MSM and non-MSM.**
- **Associations of GC incidence with sociodemographic and clinical risk factors were determined by using Cox proportional hazards regression.**
- **Up-to-date GC testing was defined as having undergone ≥ 2 GC tests from 10/1/2016 to 9/30/2017.**
- **Correlates of GC testing among HIV-positive MSM were identified by using log-linear regression.**
- **Baseline was defined as the later of first HOPS visit or 1/1/2007.**

RESULTS

- **Among 10,878 participants in the HOPS dataset as of 3/31/2018, 9,029 were seen at active or recently active sites, 4,727 had at least two HOPS visits and one CD4+ cell count/mm³ (CD4) and plasma HIV viral load test recorded since 1/1/2007.**
- **Of 4,727 eligible participants, 331 had 861 GC infections during a median follow-up of 6.3 years, with an overall incidence of 2.88 per 100 person-years. Additional results are shown in Tables 1-2 and Figure 1.**
- **During 10/1/2016 to 9/30/2017, 583 out of 1,159 HIV-positive MSM had at least one GC test. A total of 1,374 GC tests were performed on 843 patient-test dates, with 66 positive test results. Additional results are shown in Table 3 and Figures 2-4.**

Table 1. Demographic and clinical characteristics by incident GC status, the HOPS Outpatient Study, (N=4,727), 2007–2017.

Demographic and clinical characteristics	Total N (%)	No incident GC n (%)	Incident GC n (%)	P value
Total	4,727 (100.0)	4,396 (93.0)	331 (7.0)	
Age at baseline				< 0.001
18-30	656 (13.9)	543 (12.4)	113 (34.1)	
31-40	1,125 (23.8)	1,026 (23.3)	99 (29.9)	
41-50	1,835 (38.8)	1,733 (39.4)	103 (31.1)	
51+	1,111 (23.5)	1,094 (24.9)	16 (4.8)	
Race and ethnicity				0.17
Non-Hispanic/Latino white	2,306 (48.8)	2,132 (48.5)	174 (52.6)	
Non-Hispanic/Latino black	1,630 (34.5)	1,520 (34.6)	110 (33.2)	
Hispanic/Latino	613 (13.0)	582 (13.2)	31 (9.4)	
Other race/ethnicity	178 (3.8)	162 (3.7)	16 (4.8)	
Type of HOPS site				< 0.001
Private	2,960 (62.6)	2,720 (61.9)	242 (73.1)	
Public	1,767 (37.4)	1,676 (38.1)	89 (26.9)	
HIV transmission risk group, n (%)				< 0.001
MSM	2,759 (58.4)	2,484 (56.5)	275 (83.1)	
Heterosexual male	495 (10.5)	478 (10.9)	17 (5.1)	
Heterosexual female	823 (17.4)	802 (18.2)	21 (6.3)	
PWID	334 (7.1)	330 (7.5)	4 (1.2)	
Other/unknown	316 (6.7)	302 (6.9)	14 (4.2)	
CD4 count at baseline				< 0.001
<200	1,333 (28.2)	1,275 (29.0)	58 (17.5)	
200-349	1,005 (21.3)	928 (21.1)	77 (23.3)	
350-499	937 (19.8)	867 (19.7)	70 (21.1)	
500+	1,452 (30.7)	1,326 (30.2)	126 (38.1)	
Viral load at baseline				0.027
< 200 copies/mL	2,677 (56.6)	2,506 (57.0)	172 (52.0)	
200-999	378 (8.0)	359 (8.2)	19 (5.7)	
1,000-99,999	1,231 (26.0)	1,132 (25.7)	99 (29.9)	
≥100,000	441 (9.3)	399 (9.1)	41 (12.4)	
ART history at baseline				< 0.001
Experienced	3,460 (73.8)	3,272 (74.4)	218 (65.9)	
Naive	883 (18.7)	775 (17.6)	108 (32.6)	
Unknown	394 (7.5)	349 (7.9)	5 (1.5)	
AIDS diagnosis before baseline[1]				< 0.001
Yes	2,446 (58.7)	2,332 (53.0)	114 (34.4)	
No	2,281 (48.3)	2,064 (47.0)	217 (65.6)	
Chlamydia diagnosis before baseline[2]				< 0.001
Yes	143 (3.0)	112 (2.5)	31 (9.4)	
No	4,584 (97.0)	4,284 (97.5)	300 (90.6)	
Gonorrhea diagnosis before baseline[2]				< 0.001
Yes	206 (4.4)	156 (3.5)	50 (15.1)	
No	4,521 (95.6)	4,240 (96.5)	281 (84.9)	
Syphilis diagnosis before baseline[3]				< 0.001
Yes	488 (10.3)	405 (9.2)	81 (24.5)	
No	4,241 (89.7)	3,991 (90.8)	250 (75.5)	

Abbreviations: ART, antiretroviral therapy; GC, gonococcal; MSM, men who have sex with men; PWID, persons who inject drugs.
[1] AIDS determined by diagnosis.
[2] Chlamydia and gonorrhea determined by diagnosis, positive laboratory results, or treatment.
[3] Syphilis determined by diagnosis or treatment.
Baseline date is the later of first HOPS visit or January 1, 2007.

Table 2. GC incidence rates and rate ratios, the HIV Outpatient Study, (N=4,727), 2007–2017.

Demographic and clinical characteristics	Years follow-up	Cases	Incidence rate/100 PY	Univariate RR (95% CI)	Multivariable aRR (95% CI)	P value
Total	29,959.7	861	2.88			
Age at baseline						
18-30	3,344.2	311	9.30	15.33 (11.18-21.03)	7.44 (5.30-10.43)	< 0.001
31-40	7,227.5	261	3.61	5.95 (4.33-8.20)	4.62 (3.33-6.40)	< 0.001
41-50	12,079.4	245	2.03	3.34 (2.43-4.61)	2.85 (2.06-3.94)	< 0.001
51+	7,258.7	44	0.61	referent	referent	
Race and ethnicity						
Non-Hispanic/Latino white	14,968.6	507	3.39	referent	referent	
Non-Hispanic/Latino black	10,026.9	251	2.50	0.74 (0.64-0.86)	0.87 (0.72-1.05)	0.15
Hispanic/Latino	3,809.8	73	1.92	0.57 (0.44-0.72)	0.70 (0.54-0.90)	0.006
Other	1,104.4	30	2.72	0.80 (0.55-1.16)	0.92 (0.63-1.34)	0.66
Type of HOPS site						
Private	18,527.6	627	3.38	referent	referent	
Public	11,382.1	234	2.06	0.61 (0.53-0.71)	0.77 (0.64-0.94)	0.008
HIV transmission risk group						
MSM	17,138.4	753	4.39	referent	referent	
Heterosexual male	2,998.2	43	1.44	0.33 (0.24-0.44)	0.52 (0.38-0.72)	< 0.001
Heterosexual female	5,548.7	32	0.58	0.13 (0.09-0.19)	0.17 (0.12-0.23)	< 0.001
PWID	2,249.7	13	0.58	0.13 (0.08-0.23)	0.34 (0.19-0.59)	< 0.001
Other/unknown	1,976.7	20	1.01	0.23 (0.15-0.36)	0.35 (0.22-0.55)	< 0.001
CD4 count at baseline						
<200	8,509.3	130	1.53	0.39 (0.32-0.47)	0.74 (0.58-0.95)	0.019
200-349	6,491.9	205	3.16	0.80 (0.68-0.95)	1.02 (0.85-1.23)	0.80
350-499	5,790.5	174	3.00	0.74 (0.62-0.89)	0.80 (0.66-0.96)	0.017
500+	8,938.0	352	3.94	referent	referent	
Viral load at baseline						
< 200 copies/mL	18,023.5	445	2.47	0.55 (0.44-0.68)	0.74 (0.57-0.97)	0.027
200-999	2,592.3	53	2.04	0.45 (0.33-0.63)	0.80 (0.57-1.14)	0.22
1,000-99,999	7,021.1	261	3.72	0.83 (0.66-1.04)	0.88 (0.68-1.09)	0.23
≥100,000	2,272.9	102	4.49	referent	referent	
ART history at baseline						
Experienced	23,400.9	566	2.42	referent	referent	
Naive	4,784.1	286	5.98	2.50 (2.17-2.88)	1.02 (0.83-1.27)	0.84
Unknown	1,724.8	9	0.52	0.21 (0.11-0.41)	0.13 (0.07-0.26)	< 0.001
AIDS diagnosis before baseline[1]						
Yes	16,197.8	262	1.62	referent	referent	
No	13,711.9	599	4.37	2.70 (2.34-3.12)	1.45 (1.21-1.75)	< 0.001
Chlamydia diagnosis before baseline[2]						
Yes	942.6	118	12.52	4.88 (4.02-5.93)	2.77 (2.22-3.45)	< 0.001
No	28,967.1	743	2.56	referent	referent	
Gonorrhea diagnosis before baseline[2]						
Yes	1,378.7	157	11.39	4.61 (3.88-5.49)	2.38 (1.95-2.92)	< 0.001
No	28,531.0	704	2.47	referent	referent	
Syphilis diagnosis before baseline[3]						
Yes	3,093.3	231	7.47	3.18 (2.73-3.70)	1.85 (1.58-2.18)	< 0.001
No	26,816.5	630	2.35	referent	referent	

Abbreviations: aRR, adjusted rate ratio; ART, antiretroviral therapy; MSM, men who have sex with men; PWID, persons who inject drugs; PY, person-years; RR, rate ratio.
[1] AIDS determined by diagnosis. [2] Chlamydia and gonorrhea determined by diagnosis, positive laboratory results, or treatment.
[3] Syphilis determined by diagnosis or treatment.
Baseline date is the later of first HOPS visit or January 1, 2007.
Note: Baseline payer, HOPS entry year, and HCV diagnosis before baseline were included in the analyses, but are not shown in this table.

Table 3. Unadjusted and adjusted percentages of GC testing among MSM, the HIV Outpatient Study, (N=1,159), 10/1/2016–9/30/2017.

Demographic and clinical characteristics	Overall N	Overall %	GC Testing # Tested	GC Testing Unadjusted %	GC Testing 95% CI	GC Testing aPR	GC Testing 95% CI	GC Testing P value
Total	1,159	100.0	582	50.3	47.4-53.2			
Age at baseline								
18-30	120	10.3	90	75.0	66.7-82.1	1.74	1.51-1.99	< 0.001
31-40	174	15.0	103	59.2	51.8-66.3	1.37	1.18-1.60	< 0.001
41-50	265	22.9	131	49.4	43.4-55.4	1.15	0.98-1.33	0.10
51+	600	51.8	259	43.2	39.2-47.2	1.00	referent	referent
Race and ethnicity								
Non-Hispanic/Latino white	702	60.6	329	46.9	43.2-50.6	1.00	referent	referent
Non-Hispanic/Latino black	304	26.2	172	56.6	51.0-62.1	1.21	1.06-1.37	0.006
Hispanic/Latino	115	9.9	60	52.2	43.1-61.2	1.11	0.92-1.35	0.34
Other	38	3.3	22	57.9	41.9-72.7	1.24	0.93-1.64	0.25
Type of HOPS site								
Private	800	69.0	343	42.9	39.5-46.3	1.00	referent	referent
Public	359	31.0	240	66.9	61.9-71.6	1.58	1.42-1.76	< 0.001
CD4 count at baseline								
<200	59	5.1	27	45.8	33.4-58.5	0.91	0.68-1.21	0.60
200-349	110	9.5	51	46.4	37.2-55.7	0.92	0.75-1.14	0.51
350-499	204	17.6	110	53.9	47.1-60.7	1.07	0.93-1.24	0.39
500+	786	67.8	395	50.3	46.8-53.8	1.00	referent	referent
Viral load at baseline								
< 200 copies/mL	325	28.0	157	48.3	42.9-53.7	0.94	0.80-1.11	0.55
200-999	76	6.6	27	35.5	25.4-46.7	0.69	0.50-0.96	0.023
1,000-99,999	502	43.3	268	53.4	49.0-57.7	1.04	0.90-1.21	0.62
≥100,000	256	22.1	131	51.2	45.1-57.3	1.00	referent	referent
Current ART status								
Experienced	1,114	96.1	554	49.7	46.8-52.7	1.00	referent	referent
Naive	31	2.7	21	67.7	50.0-82.3	1.56	1.27-1.93	0.007
Unknown	14	1.2	8	57.1	31.2-80.4	0.89	0.53-1.50	0.84
Ever diagnosed with AIDS								
Yes	629	54.3	303	48.2	44.3-52.1	0.91	0.81-1.02	0.13
No	530	45.7	280	52.8	48.6-57.1	1.00	referent	referent
Ever diagnosed with chlamydia								
Yes	193	16.7	136	70.5	63.7-76.6	1.52	1.36-1.71	< 0.001
No	966	83.3	447	46.3	43.1-49.4	1.00	referent	referent
Ever diagnosed with gonorrhea								
Yes	175	15.1	129	73.7	66.8-79.8	1.60	1.43-1.79	< 0.001
No	984	84.9	454	46.1	43.0-49.3	1.00	referent	referent
Ever diagnosed with syphilis								
Yes	337	29.1	202	59.9	54.6-65.1	1.29	1.15-1.45	< 0.001
No	822	70.9	381	46.4	43.0-49.8	1.00	referent	referent

Abbreviations: aPR, adjusted prevalence ratio; ART, antiretroviral therapy; CI, confidence interval.
Note: Baseline payer, HOPS entry year, and HCV diagnosis before baseline were included in the analyses, but are not shown in this table.

Figure 1: GC testing and incidence rates by year among non-MSM and MSM, the HIV Outpatient Study, (N=4,727), 2007–2017.

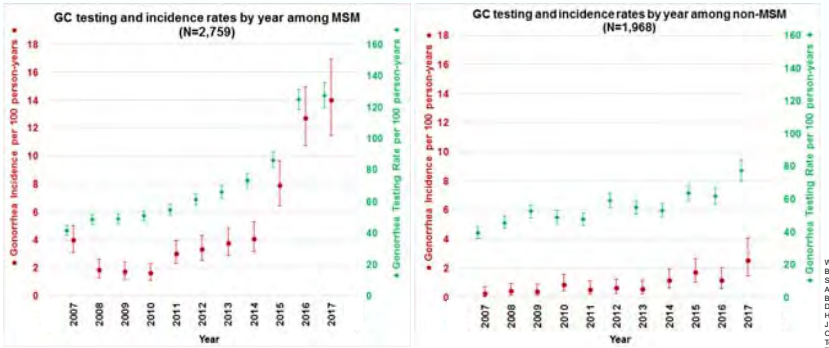


Figure 2: GC testing frequency among MSM with GC tests, 10/1/2016–9/30/2017, the HIV Outpatient Study (N=583).

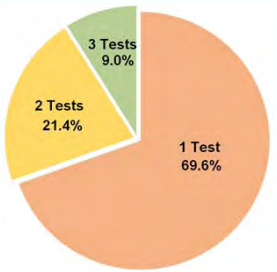


Figure 3: Percent positive of GC test results by patient-test date among MSM, 10/1/2016–9/30/2017, the HIV Outpatient Study (N=843).

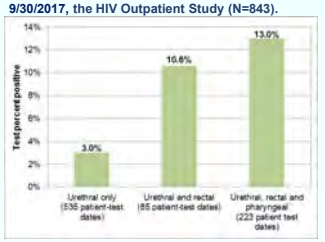
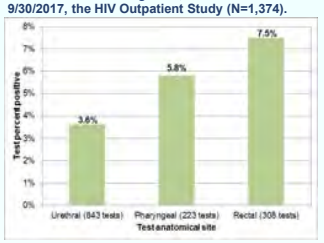


Figure 4: Percent positive of GC test results by anatomical site among MSM, 10/1/2016–9/30/2017, the HIV Outpatient Study (N=1,374).



LIMITATIONS

- **We did not have detailed information of sexual activity. Some participants who were not sexually active may not have required GC testing per recommendations [1]. Thus, we may have underestimated GC testing rates.**
- **We could not distinguish screening tests (for asymptomatic patients) from diagnostic tests (for symptomatic patients) and tests for cure. We may have overestimated GC testing rates.**
- **Our results relied on data from nine HOPS clinics, limiting its generalizability to other clinics (e.g., women's HIV clinics) or PWLH not engaged in HIV care.**

CONCLUSIONS

- **GC incidence and testing rates have increased among HIV-positive MSM and non-MSM during 2007-2017. The increase in testing might partially explain the increase in incidence.**
- **Incident GC cases were disproportionally represented by younger patients, MSM, and patients with prior STD diagnoses, suggesting interventions and treatment strategies targeting these groups are needed to minimize the risk of GC acquisitions and downstream complications.**
- **Only 50% of HIV-positive MSM were tested for GC in the prior 12 months. GC testing was significantly higher among persons of younger age, non-Hispanic black race, and with prior STD diagnoses. Only 30% of HIV-positive MSM with GC tests had up-to-date GC testing. Suboptimal testing rates for GC may indicate missed opportunities for prompt STD identification and treatment and, therefore, subsequent HIV and STD prevention.**
- **Urethral-based testing only would substantially miss anorectal and pharyngeal GC infections in HIV-positive MSM, given the substantially higher rates of GC testing positive in anorectal and pharyngeal sites. Three-site testing demonstrated a higher positive rate than 2-site (urethral and anorectal) and urethral testing only. To promote sexual health and STD prevention among PWLH, including MSM, more GC testing across anatomic sites is needed.**

REFERENCES

1. **Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2015. Atlanta: US Department of Health and Human Services; 2016.**

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