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High incidence of extra-genital gonorrheal and chlamydial infections among high-risk men who have sex with men and transgender women in Peru

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Abstract

Extra-genital *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections are associated with antimicrobial resistance and HIV acquisition. We analyzed data from a cohort of men who have sex with men (MSM) and transgender women followed quarterly for two years in Peru. Incident cases were defined as positive *N. gonorrhoeae* or *C. trachomatis* nucleic acid tests during follow-up. Repeat positive tests were defined as reinfection among those with documented treatment. We used generalized estimating equations to calculate adjusted incidence rate ratios (aIRRs). Of 404 participants, 22% were transgender. Incidence rates of rectal *N. gonorrhoeae* and *C. trachomatis* infection were 28.1 and 37.3 cases per 100 person-years, respectively. Incidence rates of pharyngeal *N. gonorrhoeae* and *C. trachomatis* infection were 21.3 and 9.6 cases per 100 person-years, respectively. Incident HIV infection was associated with incident rectal (aIRR = 2.43; 95% CI 1.66–3.55) *N. gonorrhoeae* infection. Identifying as transgender versus cisgender MSM was associated with incident pharyngeal *N. gonorrhoeae* (aIRR = 1.85; 95% CI 1.12–3.07) infection. The incidence of extra-genital *N. gonorrhoeae* and *C. trachomatis* infections was high in our population. The association with incident HIV infection warrants evaluating the impact of rectal *N. gonorrhoeae* screening and treatment on HIV transmission.

Keywords

Neisseria gonorrhoeae, *Chlamydia trachomatis*, South America, men who have sex with men, transgender women

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Introduction

Neisseria gonorrhoeae and *Chlamydia trachomatis* infections are among the most prevalent bacterial sexually transmitted infections (STIs) worldwide, and despite control and prevention efforts, the incidence of these infections has been increasing.[1] Studies from Peru among men who have sex with men (MSM) and transgender women have found a prevalence of rectal *N. gonorrhoeae* and *C. trachomatis* infections between 4.8 and 8.8% and 13.7 and 19.0%, respectively.[2,3] The incidence of rectal *N. gonorrhoeae* and *C. trachomatis* infection among a community-based population of MSM and transgender women in Peru has been reported to be as high as 10.1 and 16.3 per 100 person-years, respectively, while the incidence of pharyngeal *N. gonorrhoeae* and *C. trachomatis* infection has been reported to be as high as 7.8 and 3.4 per 100 person-years, respectively.[4]

The consequences of extra-genital infections can be profound. One study demonstrated that the risk of HIV acquisition increased eightfold after two rectal

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infections with either *N. gonorrhoeae* or *C. trachomatis* within two years.[5] Furthermore, the prevalence of antimicrobial resistant *N. gonorrhoeae* has been shown to be higher among pharyngeal infections,[6,7] perhaps contributing to the emergence of multidrug-resistant *N. gonorrhoeae* infections,[8] an urgent public health issue.[9]

The World Health Organization (WHO) recommends periodic testing for rectal *N. gonorrhoeae* and *C. trachomatis* infections among MSM and transgender women.[10] However, periodic testing for rectal *N. gonorrhoeae* and *C. trachomatis* is not yet included in the national guidelines of Peru[11] and other countries due to gaps in laboratory equipment and uncertainty about the cost-effectiveness. Furthermore, additional incidence data in various populations will be useful to support STI screening recommendations. Given the previously reported high incidence of extra-genital *N. gonorrhoeae* and *C. trachomatis* infections, as well as the consequences of these infections, we aimed to characterize the incidence of these infections among a high-risk cohort of MSM and transgender women in Lima, Peru.

Methods

The PICASSO study[12] is a prospective cohort study of MSM and transgender women in Lima, Peru, with the objective of characterizing the frequency of syphilis and repeat infection or treatment failure among that population. Participants were recruited from one of two clinic sites in Lima: one a government-run STI clinic for key populations (Alberto Barton STD Clinic), and the other a nongovernmental organization gay men's community center (Epicentro), both located in Metropolitan Lima. Participants met high-risk criteria for syphilis based on risk factors previously reported in Deiss et al.,[12] which was defined as the presence of at least three of the following reported at the time of screening: HIV infected, a history of syphilis in the prior two years, any current ulcerative STI, any STI diagnosed in the prior six months, more than five years of sexual activity, and, over the preceding three months, more than five sex partners, or more than five occurrences of condomless anal sex. Enrollment and follow-up took place between June 2013 and July 2016. Regular follow-up reminders were provided via cell-phone text messages, phone calls, e-mail, and Internet chats to augment retention.[13,14]

Participants answered a standardized, computer-based survey at baseline and during follow-up visits at three-month intervals for 24 months. That follow-up period was defined by the parent cohort.[12] The survey collected sociodemographic information such as age, monthly income, alcohol and substance use, sexual identity, and gender identity. Questions of sexual behavior over the preceding three months included sex role (insertive, receptive, or versatile) for anal and oral sex, condom use, and number of male sex partners. We also asked for history of current/past STIs, including HIV. High-risk alcohol use was defined as a score of ≥ 8 on the Alcohol Use Disorder Identification Tool,[15] which has been associated with high-risk sexual behavior.[16]

Each study visit also included laboratory testing for HIV, *Treponema pallidum*, *N. gonorrhoeae*, and *C. trachomatis* infections. HIV testing was performed with the Greenscreen™ ULTRA HIV Ag-Ab Assay (Bio-Rad Laboratories, Inc., Hercules, CA, USA). Incident HIV infection was defined as a newly-positive HIV test during follow-up. Pretest counseling was provided to participants, and participants diagnosed with HIV infection were referred to the Peruvian National HIV Treatment Program. Self-collected rectal and staff-collected pharyngeal Dacron swabs from the Aptima Combo 2 assay kits (Hologic®, San Diego, CA, USA) were tested for *N. gonorrhoeae* and *C. trachomatis* using nucleic acid amplification tests by the Aptima Combo 2 assay. Participants diagnosed with *C. trachomatis* infection were offered treatment with a one-time oral dose of azithromycin, 1000 mg, in accordance with Peruvian National STI Treatment Guidelines[11]; however, the treatment for *N. gonorrhoeae* differed by clinic. The Alberto Barton STD clinic complied with national Peruvian guidelines by offering ciprofloxacin 500 mg orally, whereas Epicentro offered ceftriaxone 250 mg injection due to concerns of ciprofloxacin-resistant *N. gonorrhoeae* infections.[17,18] Incident cases were defined among participants with positive *N. gonorrhoeae* or *C. trachomatis* nucleic acid amplification tests during follow-up with no prior infection or who had documented treatment of a prior infection.

We conducted an analysis of factors associated with incident *N. gonorrhoeae* and *C. trachomatis* infections from the PICASSO study using generalized estimating equations with a Poisson regression and an unstructured correlation structure to estimate adjusted incidence rate ratios (aIRR) accounting for the within-participant correlation of multiple follow-up visits. Variables found to be significant in the bivariate analysis (p-value < 0.05) were selected for multivariable modeling. We analyzed the number of male sex partners as a categorical variable (0, 1, 2–3, 4–9, ≥ 10). We used a backwards-stepwise approach to determine the final multivariable model. All models controlled for the number of male sex partners and sexual exposures in the preceding three months (receptive oral sex for pharyngeal infections and anal sex role for rectal infections).

We then developed four additional exploratory models to determine factors associated with rectal and pharyngeal infections among MSM and transgender women separately. Because of the limited number of participants who identified as transgender women, we developed those models evaluating factors associated with infection by anatomic site, instead of by both infectious organism and anatomic site. Variables found to have p-values < 0.1 in the bivariate analyses were selected for multivariable modeling. The different p-value threshold was used due to the decreased sample and power for each model. Furthermore, because of the limited sample size, we recategorized the number of recent male sex partners (0–1, 2–3, 4–9, $\geq$10). We used the same backwards-stepwise approach to develop the final multivariable models. Those models also controlled for the number of male sex partners and sexual exposures in the preceding three months (receptive oral sex for pharyngeal infections and anal sex role for rectal infections).

In addition, we performed a retention analysis using Chi square and Fisher's Exact tests, as well as Wilcoxon's Rank Sum Test for nonparametric data, comparing risk factors reported at baseline among participants who never returned after enrollment to risk factors reported at baseline by participants who missed one or zero follow-up visits. All analyses were performed using STATA software version 14.2 (StataCorp®, College Station, TX, USA).

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Results

Among 404 study participants, 125 (31%) had HIV infection at baseline. Of the 89 (22%) participants that identified as transgender women, 30 (34%) had HIV infection at baseline. The mean age of our population was 29.6 years old at baseline (SD 9.6 years). The incidence rates of rectal infection were 28.1 and 37.3 cases per 100 person-years with *N. gonorrhoeae* and *C. trachomatis*, respectively; while incidence rates of pharyngeal infection were 21.3 and 9.6 cases per 100 person-years with *N. gonorrhoeae* and *C. trachomatis*, respectively. Figure 1 shows the incidence rate of each anatomic site-specific infection comparing MSM and transgender women.

Analysis of risk factors among the entire population

Tables 1 and 2 show the results of our bivariate and multivariable modeling for risk factors associated with pharyngeal and rectal *N. gonorrhoeae* and *C. trachomatis* infections, respectively. Older age was protective against both types of rectal infection as well as pharyngeal infection with *N. gonorrhoeae*. Identifying as a transgender woman compared to a cisgender MSM was associated with pharyngeal infection with *C. trachomatis* as well as with rectal infection with

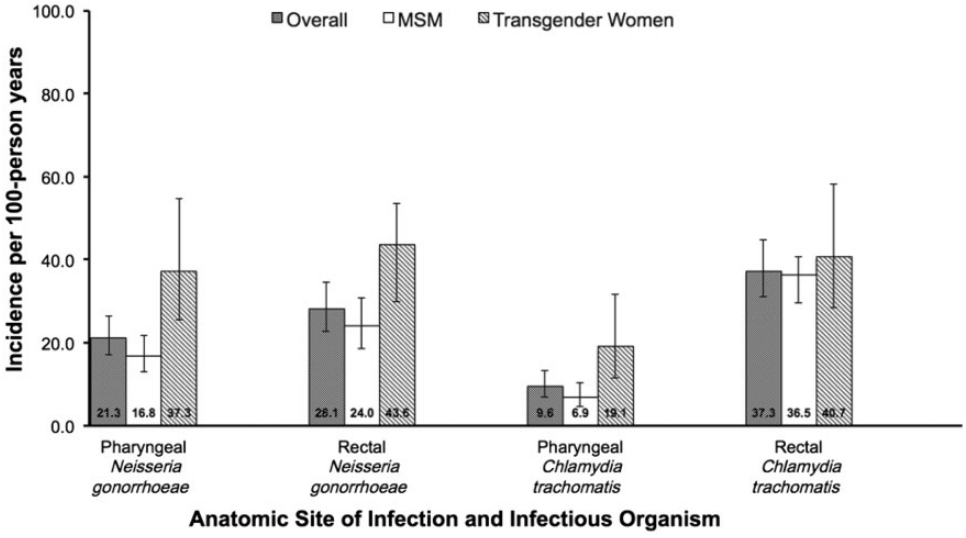

Figure 1. Incidence rates of pharyngeal and rectal *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections among men who have sex with men and transgender women in Lima, Peru enrolled between June 2013 and July 2016.
MSM: men who have sex with men.

Table 1. Incidence of pharyngeal and rectal *Neisseria gonorrhoeae* infection and associated risk factors among a cohort of men who have sex with men and transgender women at high risk for syphilis from Lima, Peru.

	Pharyngeal *Neisseria gonorrhoeae*			Rectal *Neisseria gonorrhoeae*		
	No. of incident cases	Crude IRR (95% CI)	Adjusted IRR (95% CI)[a]	No. of incident cases	Crude IRR (95% CI)	Adjusted IRR (95% CI)
Age (years)						
18–29	66	ref	ref	94	ref	ref
30–39	23	0.54 (0.31–0.93)	**0.59 (0.35–0.98)**	29	0.50 (0.30–0.83)	**0.52 (0.31–0.86)**
40–49	16	0.65 (0.37–1.17)	0.81 (0.49–1.34)	10	0.30 (0.14–0.62)	**0.41 (0.20–0.82)**
≥50	5	0.21 (0.09–0.50)	**0.26 (0.11–0.62)**	12	0.36 (0.16–0.78)	0.47 (0.22–1.01)
Incident HIV infection						
No	74	ref		69	ref	ref
Yes	36	2.71 (1.45–5.07)		76	3.12 (2.03–4.77)	**2.43 (1.66–3.55)**
Receptive anal sex with a man, past three months						
Had no sex	Not applicable	Not applicable		46	ref	
Always used condoms during sex	Not applicable	Not applicable		78	1.28 (0.90–1.83)	
Had condomless sex	Not applicable	Not applicable		21	1.36 (0.78–2.40)	
Insertive anal sex with a man, past three months						
Had no sex	Not applicable	Not applicable		94	ref	
Always used condoms during sex	Not applicable	Not applicable		34	0.69 (0.46–1.04)	
Had condomless sex	Not applicable	Not applicable		17	1.42 (0.85–2.37)	
Insertive oral sex with a man in past three months						
No	57	ref		Not applicable	Not applicable	
Yes	53	1.03 (0.70–1.52)		Not applicable	Not applicable	
Receptive oral sex with a man in past three months						
No	26	ref	ref	Not applicable	Not applicable	
Yes	84	1.75 (1.17–2.61)	1.35 (0.87–2.09)	Not applicable	Not applicable	
Antibiotic use in the past three months						
No	99	ref		121	ref	
Yes	7	0.59 (0.32–1.10)		16	0.98 (0.57–1.68)	
Transgender identity						
No	69	ref	ref	99	ref	ref
Yes	41	2.20 (1.39–3.49)	1.59 (0.97–2.60)	46	1.80 (1.15–2.84)	**1.99 (1.13–3.51)**
Anal sex role						
Insertive	13	ref		4	ref	ref
Receptive	50	1.97 (1.05–3.69)		66	6.75 (2.54–17.91)	**4.51 (1.60–12.75)**
Versatile	47	1.52 (0.82–2.81)		75	6.49 (2.40–17.55)	**5.23 (1.89–14.44)**
Performed anilingus in the past three months						
No	98	ref		130	ref	
Yes	12	0.85 (0.45–1.60)		15	0.74 (0.43–1.28)	
Number of male sex partners, past three months						
0	3	0.65 (0.19–2.25)	0.81 (0.22–2.93)	8	0.92 (0.49–1.73)	0.94 (0.51–1.73)
1	20	ref	ref	34	ref	ref
2–3	24	1.20 (0.66–2.18)	1.21 (0.68–2.12)	27	0.83 (0.48–1.41)	0.93 (0.57–1.52)
4–9	19	1.19 (0.64–2.22)	1.17 (0.67–2.06)	25	0.94 (0.57–1.58)	1.08 (0.66–1.76)
>10	43	2.25 (1.25–4.04)	1.52 (0.90–2.56)	49	1.55 (0.94–2.58)	1.51 (0.92–2.50)
High-risk alcohol use[b]						
No	66	ref		88	ref	
Yes	44	1.16 (0.81–1.66)		57	1.18 (0.86–1.61)	
Drug use prior to sex						
No	106	ref		140	ref	
Yes	4	1.84 (0.72–4.68)		5	1.43 (0.66–3.08)	
Earns less than Peruvian minimum monthly wage						
≥250 USD	65	ref		80	ref	
<250 USD	33	1.05 (0.70–1.58)		55	1.49 (1.05–2.11)	
Treatment center						
Epicentro	39	ref		79	ref	ref
Barton	71	1.41 (0.90–2.22)		66	0.65 (0.43–1.00)	**0.55 (0.34–0.88)**

CI: confidence interval; IRR: incidence rate ratio. Values in bold are statistically significant (p-value<0.05).

[a]This model was adjusted for recent rectal *Neisseria gonorrhoeae* infection.

[b]High-risk alcohol behavior was defined as a score of ≥ 8 on an alcohol AUDIT.

Table 2. Incidence of pharyngeal and rectal *Chlamydia trachomatis* infection and associated risk factors among a cohort of men who have sex with men and transgender women at high risk for syphilis from Lima, Peru.

	Pharyngeal *Chlamydia trachomatis*			Rectal *Chlamydia trachomatis*		
	No. of incident cases	Crude IRR (95% CI)	Adjusted IRR (95% CI)	No. of incident cases	Crude IRR (95% CI)	Adjusted IRR (95% CI)
Age (years)						
18–29	27	ref		112	ref	ref
30–39	7	0.41 (0.15–1.11)		49	0.72 (0.47–1.11)	0.72 (0.46–1.13)
40–49	10	1.01 (0.39–2.65)		15	0.39 (0.20–0.78)	**0.45 (0.22–0.89)**
≥50	7	0.76 (0.31–1.83)		21	0.55 (0.31–0.98)	0.61 (0.34–1.10)
Incident HIV infection						
No	33	ref		106	ref	
Yes	18	1.74 (0.71–4.28)		91	1.96 (1.32–2.91)	
Receptive anal sex with a man, past three months						
Had no sex	Not applicable	Not applicable		59	ref	
Always used condoms during sex	Not applicable	Not applicable		111	1.55 (1.12–2.16)	
Had condomless sex	Not applicable	Not applicable		27	1.62 (1.03–2.55)	
Insertive anal sex with a man, past three months						
Had no sex	Not applicable	Not applicable		113	ref	
Always used condoms during sex	Not applicable	Not applicable		64	1.00 (0.74–1.36)	
Had condomless sex	Not applicable	Not applicable		20	1.42 (0.87–2.31)	
Insertive oral sex with a man in past three months						
No	29	ref		Not applicable	Not applicable	
Yes	22	0.84 (0.47–1.48)		Not applicable	Not applicable	
Receptive oral sex with a man in past three months						
No	15	ref	ref	Not applicable	Not applicable	
Yes	36	1.41 (0.69–2.91)	1.01 (0.50–2.06)	Not applicable	Not applicable	
Antibiotic use in the past three months						
No	48	ref		169	ref	
Yes	2	0.34 (0.10–1.19)		28	0.81 (0.50–1.32)	
Transgender identity						
No	29	ref	ref	153	ref	
Yes	22	2.79 (1.46–5.33)	**2.66 (1.45–4.88)**	44	1.12 (0.74–1.70)	
Anal sex role						
Insertive	7	ref		17	ref	ref
Receptive	24	1.65 (0.60–4.52)		83	2.03 (1.13–3.63)	**1.93 (1.07–3.49)**
Versatile	20	1.18 (0.42–3.34)		95	1.78 (1.00–3.17)	1.62 (0.91–2.89)
Performed anilingus in the past three months						
No	48	ref		171	ref	
Yes	3	0.44 (0.15–1.32)		26	1.07 (0.69–1.66)	
Number of male sex partners, past three months						
0	1	0.49 (0.08–3.14)	0.54 (0.08–3.71)	13	1.43 (0.71–2.86)	1.14 (0.60–2.16)
1	9	ref	ref	39	ref	ref
2–3	14	1.60 (0.72–3.56)	1.55 (0.70–3.44)	41	1.27 (0.78–2.05)	1.34 (0.87–2.05)
4–9	9	1.30 (0.49–3.45)	1.06 (0.39–2.91)	45	1.67 (1.04–2.67)	**1.80 (1.19–2.73)**
>10	18	1.83 (0.76–4.43)	1.22 (0.53–2.82)	57	1.88 (1.12–3.18)	**2.15 (1.34–3.46)**
High-risk alcohol use[a]						
No	25	ref		129	ref	
Yes	26	1.74 (1.01–2.99)		68	0.99 (0.75–1.29)	
Drug use prior to sex						
No	48	ref	ref	191	ref	
Yes	3	3.19 (1.06–9.64)	2.85 (0.93–8.72)	6	1.30 (0.54–3.11)	
Earns less than Peruvian minimum monthly wage						
≥250 USD	30	ref		126	ref	
<250 USD	19	0.97 (0.68–1.39)		60	0.97 (0.68–1.39)	
Treatment center						
Epicentro	15	ref		111	ref	ref
Barton	36	1.96 (1.00–3.82)		86	0.65 (0.46–0.94)	**0.60 (0.41–0.89)**

CI: confidence interval; IRR: incidence rate ratio. Values in bold are statistically significant (p-value<0.05)

[a]High-risk alcohol behavior was defined as a score of ≥ 8 on an alcohol AUDIT.

N. gonorrhoeae. Furthermore, incident HIV infection was associated with both types of rectal infection.

Analysis of risk factors among MSM

In our multivariable model of risk factors associated with rectal infection, we found that higher age groups, 30–39 years (aIRR = 0.58; 95% CI 0.35–0.94) and 40–49 years (aIRR = 0.36; 95% CI 0.16–0.77), were negatively associated with infection compared to those aged between 18 and 29 years. Additionally, incident HIV infection during follow-up (aIRR = 1.91; 95% CI 1.31–2.81) and reporting an exclusively receptive (aIRR = 3.24; 95% CI 1.70–6.17) or versatile (aIRR = 2.94; 95% CI 1.63–5.32) role for anal sex compared to an exclusively insertive role were positively associated with rectal infection. In our multivariable model of risk factors associated with pharyngeal infection, we found that age between 30 and 39 years (aIRR = 0.45; 95% CI 0.25–0.81) was negatively associated with infection compared to age between 18 and 29 years.

Analysis of risk factors among transgender women

In our multivariable model of risk factors for rectal infection, we found that higher age groups, 30–39 years (aIRR = 0.51; 95% CI 0.29–0.92) and ≥50 years (aIRR = 0.35; 95% CI 0.14–0.87) were protective compared to age between 18 and 29 years. In our multivariable model of risk factors for pharyngeal infection, we similarly found that higher age groups, 30–39 years (aIRR = 0.50; 95% CI 0.28–0.91) and ≥50 years (aIRR = 0.22; 95% CI 0.06–0.83), were protective compared to age between 18 and 29 years. Furthermore, in the prior three months, reporting insertive oral sex (aIRR = 1.71; 95% CI 1.05–2.79), drug use before to sex (aIRR = 4.03; 95% CI 1.64–9.91), 2–3 male sex partners (aIRR = 4.41; 95% CI 1.01–19.21), or ≥ 10 male sex partners (aIRR = 4.14; 95% CI 1.17–14.69) compared to reporting zero or one male sex partner were risk factors for infection. Appendices 1 and 2 provide the complete results of our multivariable models of risk factors among MSM and transgender women, respectively.

Retention analysis

After baseline enrolment, only 42 (10%) participants did not return for any follow-up visits. Figure 2 shows the result of our retention analysis.

Discussion

Our results demonstrate the high incidence of extragenital *N. gonorrhoeae* and *C. trachomatis* infections among MSM and transgender women in Lima, Peru. Our results also add to the paucity of data specific to transgender women.[19] The incidence of both infections was higher in our population than was previously reported among MSM and transgender women in Peru,[4] and from other countries,[20,21] which is likely due to the high-risk inclusion criteria for the present study.[12] Because of the select high-risk study population, our findings might not be generalizable to other populations.

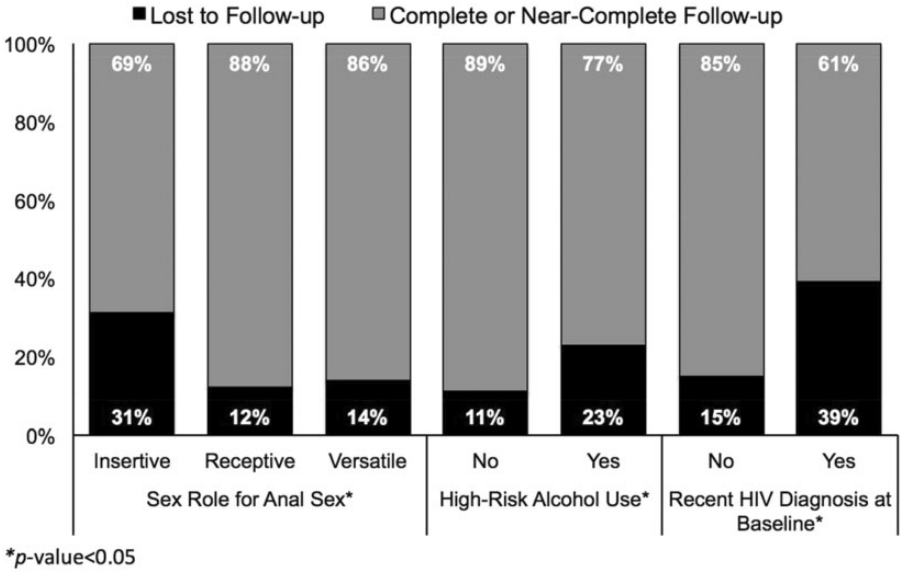

Figure 2. Risk factors associated with 0–1 follow-up visits compared to 7–8 (complete or near-complete) follow-up visits among a cohort of high-risk MSM and transgender women in Lima, Peru.

The WHO recommends periodic testing for rectal *N. gonorrhoeae* and *C. trachomatis* infections among MSM and transgender women,[10] with the caveat that data to support the impact of such a recommendation are limited. Nucleic acid amplification testing, however, is expensive and may not be feasible in resource-limited settings. Therefore, the use of certain criteria to identify high-risk behavior in order to better target screening efforts, as was done in this study, may improve the cost-effectiveness of periodic testing for rectal STIs. Such efforts to target screening are similar to what has been reported in studies attempting to focus HIV screening among serodiscordant couples[22] and among African women.[23]

Screening for rectal STIs may contribute to the prevention of HIV infection, as rectal *N. gonorrhoeae* or *C. trachomatis* infection has been shown to predispose to HIV infection,[5,24,25] which is consistent with our finding that rectal *N. gonorrhoeae* infection was associated with incident HIV infection; however, we are unable to make a definitive determination regarding the timing of each infection with our current data. One community-based study estimated that preventing a preceding rectal STI would have prevented 15% of HIV infections in their population.[26] Furthermore, a recent modeling study concluded that screening for rectal *N. gonorrhoeae* and *C. trachomatis* infections might be a cost-effective method for preventing HIV transmission.[27]

In addition to shared behavioral risk factors for rectal STI and HIV acquisition, rectal STIs are thought to confer a biologic susceptibility to HIV acquisition due in part to the loss of mucosal integrity as well as increased local inflammation leading to an increased presence of cells susceptible to HIV infection.[28,29] Additionally, a prior study demonstrated that the pro-inflammatory cytokines produced in response to *N. gonorrhoeae* infection enhance HIV replication *in vitro*.[30] Further research is warranted to investigate the impact of rectal STI screening and treatment on the incidence of HIV infection.

The high incidence of pharyngeal infection in our population supports the consideration of periodic testing for pharyngeal infections in future recommendations. The pharynx has been shown to be a reservoir for antimicrobial resistance[7,8,31] and the source of transmission for a high proportion of urethral infections.[32] Effective treatment and prevention strategies for pharyngeal infections, therefore, may be an important approach in the prevention of multidrug-resistant *N. gonorrhoeae*, one of the top three urgent antimicrobial resistant threats to public health.[33]

The separate analyses among MSM and transgender women were conducted to assess differences in risk factors between these populations. While the small number of transgender women in our population limited that analysis, we found that drug use prior to sex was associated with pharyngeal *N. gonorrhoeae* or *C. trachomatis* infection among transgender women, but not among MSM. There are known differences in sexual practices between cisgender MSM and transgender women.[19,34] A higher rate of oral sex after drug use among transgender women compared to MSM may explain our finding. In addition, we found a higher overall incidence of pharyngeal infections among transgender women compared to cisgender MSM in our population, which is consistent with prior reports.[2,4]

Younger age was associated with increased risk for pharyngeal and rectal infection with either *N. gonorrhoeae* or *C. trachomatis* among both MSM and transgender women. Those findings are consistent with previous reports[2–4,35] and may be due in part to a greater number of sexual contacts and increased rates of risky behavior such as casual sex among younger populations compared to older populations.[36,37] Our models controlled for both the number of male sex partners and types of sexual activity; however, we did not control for condom use. Therefore, lower rates of condom use may explain the higher incidence of infections among younger participants in our population.

We found no difference in incidence rates of pharyngeal infections among those treated at the government-run clinic versus the non-government-run clinic, though we did find a lower incidence of rectal infections with either *N. gonorrhoeae* or *C. trachomatis* at the government-run clinic. One likely explanation may be issues of sexual network differences influencing the underlying risk of infection between the populations that access the two different clinics, which were not observable in our data. However, as we were only comparing two clinics, additional studies would be needed to replicate and validate our results. The observed difference in the incidence of rectal infection was not likely due to the different treatment regimens for *N. gonorrhoeae* infection, as we found a similar difference in the incidence rate of rectal *C. trachomatis* infection of rectal *C. trachomatis* infection even though both clinics used the same treatment regimen for *C. trachomatis* infection. Without microbiologic data, we cannot make inferences into the influence of antimicrobial resistance on *N. gonorrhoeae* incidence, which should be the foundation of future studies.

Limitations

A limitation of this study is that it was conducted solely among high-risk MSM and transgender women, and therefore the results may not be generalizable to lower-risk MSM and transgender women. Additionally, we did not perform confirmatory testing of *N. gonorrhoeae* or *C.*

trachomatis with a second nucleic acid amplification test, leaving the potential for some false positive results. Another limitation is that our study may have been underpowered to demonstrate significant associations with the outcomes described above, likely due to the number of potential risk factors included. Larger studies will help to improve the precision of our findings. Similarly, the number of transgender women in our population limited our power to analyze risk factors within that population alone.

Furthermore, our retention analysis demonstrated that a higher proportion of participants who were lost to follow-up reported exclusively insertive anal sex, high-risk alcohol use behavior, or a recent diagnosis of HIV infection at baseline. Participants reporting exclusively insertive anal sex were likely in a lower risk category for STIs; therefore, our results may have slightly overestimated the incidence of infection. On the other hand, participants reporting high-risk alcohol use behavior and a recent diagnosis of HIV infection at baseline were likely in a higher risk category for STIs, thus potentially causing us to underestimate the incidence of infection. However, since the number of participants lost to follow-up was a small proportion of the overall population, our results were likely not significantly impacted.

Conclusion

Our findings demonstrate the high incidence of extragenital *N. gonorrhoeae* and *C. trachomatis* infections among high-risk MSM and transgender women in Lima, Peru, and add important data on transgender women to the literature. The high incidence of rectal infection supports the WHO recommendation of periodic nucleic acid amplification screening for rectal *N. gonorrhoeae* and *C. trachomatis* infections among MSM and transgender women, and the association with incident HIV infection warrants evaluating the impact of *N. gonorrhoeae* and *C. trachomatis* screening and treatment on HIV incidence. The high incidence of pharyngeal infection also warrants further assessment of the value of periodic screening for pharyngeal infections among MSM and transgender women.

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