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SHORT REPORT

Serosorting and recreational drug use are risk factors for diagnosis of genital infection with chlamydia and gonorrhoea among HIV-positive men who have sex with men: results from a clinical cohort in Ontario, Canada

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ABSTRACT

Objectives Rates of chlamydia and gonorrhoea have been rising in urban centres in Canada, particularly among HIV-positive men who have sex with men (MSM). Our objective was to identify behavioural risk factors for diagnosis with chlamydia and gonorrhoea in this population, with a focus on the HIV status of sexual partners.

Methods The OHTN Cohort Study follows people in HIV care across Ontario. We restricted the analysis to 1997 MSM who completed questionnaires in 2010–2013 at one of seven clinics that submit all chlamydia and gonorrhoea tests to the provincial public health laboratory; we obtained test results via record linkage. We estimated cumulative incidences using Kaplan–Meier methods and identified risk factors for diagnosis of a composite outcome (chlamydia or gonorrhoea infection) using Cox regression.

Results At follow-up, there were 74 new chlamydia/gonorrhoea diagnoses with a 12-month cumulative incidence of 1.7% (95% CI 1.1% to 2.2%). Risk factors for chlamydia/gonorrhoea diagnosis were: 5+ HIV-positive partners (HR=3.3, 95% CI 1.4 to 7.8; reference=none) and recreational drug use (HR=2.2, 95% CI 1.2 to 3.9).

Conclusions Heightened risks with recreational drug use and multiple HIV-positive partners suggest that chlamydia/gonorrhoea may have achieved high prevalence in certain sexual networks among HIV-positive MSM. Interventions to promote safer sex and timely testing among MSM are needed.

INTRODUCTION

Rates of chlamydia and gonorrhoea have risen in urban centres in Canada including an increase in case reports among men who have sex with men (MSM).[1] Coinfection with HIV is particularly concerning because sexually transmitted infections (STIs) can increase likelihood of HIV transmission.[1] In Ontario, Canada, we previously reported demographic and clinical risk factors for new chlamydia and gonorrhoea diagnoses among an HIV clinical cohort followed from 2008 to 2011.[2] Risk was highest among MSM, particularly among younger MSM and (for gonorrhoea) among MSM with unsuppressed viral load, with little variation between ethnic groups.[2] However, full characterisation of risk requires examination of behavioural risk factors since sexual behaviour and prevalence in sexual networks drive STI risk. 'Serosorting', selecting sexual partners of the same HIV serostatus, could raise STI risk since condoms may be used less frequently, which could concentrate infection in sexual networks of HIV-positive persons.[3] Recreational drug use has also been linked to sexual risk taking.[1 4 5] Our objective was to extend our previous analysis by longitudinally exploring behavioural risk factors for diagnoses of genital chlamydia and gonorrhoea infection among HIV-positive MSM attending HIV care in Ontario, specifically focusing on the risks associated with serosorting and recreational drug use.

METHODS

We analysed data from the Ontario HIV Treatment Network Cohort Study (OCS) which follows persons attending 10 HIV clinics across Ontario. The province has publicly funded, universal access to medically necessary healthcare. The OCS has been described in detail elsewhere[6] and received ethical approval from the University of Toronto HIV Research Ethics Board (protocol reference 23954) and participating sites. Participation is voluntary. Data were collected through chart review, annual interviews and record linkage with the Public Health Ontario Laboratories (PHOL). At PHOL, simultaneous cotesting of chlamydia and gonorrhoea urine specimens was done by nucleic acid amplification testing using the Gen-Probe Aptima assay (Gen-Prose, San Diego, California, USA). Canadian guidelines recommend chlamydia and gonorrhoea testing annually for MSM at ongoing risk, regardless of HIV status.[1]

Our focus was on sexual behaviour and recreational drug use risk factors, adjusting for age, region and time-updated viral load as potential confounders. Men reported recreational drug use

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Table 1 Characteristics of HIV-positive men who have sex with men (MSM) at completion of their first sexual behaviour questionnaire, OHTN Cohort Study, 2010–2013

Total N	1997 (100%)
Mean age at baseline (SD)	47.7 (10.2)
Self-reported sexual orientation	
Gay	1767 (88.5%)
Bisexual	151 (7.6%)
Heterosexual	58 (2.9%)
Unknown*	21 (1.1%)
Race/ethnicity	
White	1492 (74.7%)
Black/African	80 (4.0%)
Mixed race/ethnicity	168 (8.4%)
Indigenous	85 (4.3%)
Other	170 (8.5%)
Education	
High school or less	448 (22.4%)
Some postsecondary	435 (21.8%)
Completed postsecondary	1111 (55.6%)
Annual personal income	
<$C20 000	702 (35.2%)
$C20 000–$C59 999	794 (39.8%)
≥$C60 000	470 (23.5%)
Unknown	31 (1.6%)
Region where receiving HIV care	
Toronto	1703 (85.3%)
Other	294 (14.7%)
Year of HIV diagnosis	
Prior to 2000	1129 (56.5%)
2000–2009	737 (36.9%)
2010 or later	131 (6.6%)
Median (IQR)	1997 (1991–2005)
HIV clinical status	
Initiated antiretroviral treatment	1647 (82.5%)
Mean CD4 cell count/mm^3 (SD)	537 (253)
Undetectable viral load (<40 copies/mL)	1568 (78.5%)
Recreational drug use in the preceding 6 months	
Any†	418 (20.9%)
Methamphetamines	188 (9.4%)
Cocaine	205 (10.3%)
Club drugs‡	217 (10.9%)
Other§	187 (9.4%)
Multiple (two or more)	232 (11.6%)
Sexual behaviours in the preceding 3 months	
Number of sexual partners	
None	710 (35.6%)
One	535 (26.8%)
Two to four	452 (22.6%)
Five or more	274 (13.7%)
Number of HIV-positive partners	
None	1210 (60.6%)
One	330 (16.5%)
Two to four	255 (12.8%)
Five or more	100 (5.0%)
Number of HIV-negative/status unknown partners	
None	1101 (55.1%)
One	364 (18.2%)
Two to four	229 (11.5%)
Five or more	214 (10.7%)
Anal sex	
No partner	710 (35.6%)
Sexually active but no anal sex	319 (16.0%)
Anal sex always with a condom	349 (17.5%)
Any condomless anal sex	551 (27.6%)
Anal sex with HIV-positive partners¶	
No HIV-positive partners	1210 (60.6%)
Sexually active but no anal sex	124 (6.2%)
Anal sex always with a condom	147 (7.4%)
Any condomless anal sex	416 (20.8%)
Anal sex with HIV-negative/status unknown partners¶	
No HIV-negative/status unknown partners	1101 (55.1%)
Sexually active but no anal sex	214 (10.7%)
Anal sex always with a condom	347 (17.4%)
Any condomless anal sex	257 (12.9%)

*Only 0.1% of the sample had missing data for race/ethnicity and 0.2% for education.
†Any recreational drug use includes anabolic steroids, amphetamines, methamphetamines, cocaine, crack/freebase, club drugs, heroin, other opiates, tranquilisers and other drugs, except cannabis as it was unmeasured for 4/7 participating clinic sites.
‡Club drugs include Ecstasy/MDMA (3,4-methylenedioxy-methamphetamine), Special K (ketamine), GHB (γ hydroxybutyrate), PCP (phencyclidine) and poppers (amyl nitrite).
§Other includes anabolic steroids, amphetamines, crack/freebase, heroin, other opiates, tranquilisers and 'other' option in drug use section of questionnaire.
¶Serostatus-specific variables were not mutually exclusive. The sexual behaviour questionnaire had a series of questions for HIV-positive partners followed by questions specific to HIV-negative/status unknown partners allowing for the capture and coding of different sexual practices by HIV status of partners.

in face-to-face interviews. Next, they self-completed a computerised sexual behaviour questionnaire without interviewers present.

As of 12/2013, there were 6408 enrolees. Our analysis included 1997 male participants reporting non-heterosexual orientation or sex with men as an HIV risk factor; self-completed at least one sexual behaviour questionnaire between 2010 and 2013 and attended one of seven clinics that submitted all chlamydia and gonorrhoea tests to PHOL, the primary provider for chlamydia and gonorrhoea tests for sexual health clinics (HIV specialty and primary care clinics may also send specimens to private laboratories).

We conducted all statistical analyses using SAS V.9.3 (SAS Institute, Cary, North Carolina, USA). p Values were two-sided and statistical significance was determined using the p value of <0.05. We used Kaplan–Meier methods to estimate the cumulative incidence proportions tested for or diagnosed with chlamydia or gonorrhoea following completion of the first sexual behaviour questionnaire. As previously done, diagnosis rates were calculated among tested and untested participants[2] thus underestimating true incidence since asymptomatic infections among those untested are excluded from the numerator.

For risk factor analysis, we grouped chlamydia and gonorrhoea into a composite outcome to improve statistical power and because their modes of transmission and clinical/public health implications are similar; HR estimates for separate chlamydia and gonorrhoea outcomes were not meaningfully different. For men diagnosed more than once, we selected the earliest event, which occurred rarely. We excluded participants with missing data (1.3% of observations) and two cases with zero event times. Men with no events were censored using the earliest of the dates of loss to follow-up, death or 31 December 2013.

RESULTS

At completion of their first sexual behaviour questionnaire, men were aged 48 years, on average (table 1). The median number of years since HIV diagnosis was 18 (IQR 10–24). The majority (64.4%) were sexually active in the preceding 3 months, whereas a minority (20.9%) reported recreational drug use (table 1).

Men were followed a median of 2.9 years (IQR 1.8–3.3) for a sum of 5833 person-years. The Kaplan–Meier cumulative probabilities of testing for chlamydia/gonorrhoea were 24.6% at 12 months and 33.1% at 24 months. In all, 35.1% (700/1997) were tested over the entire course of follow-up. The majority of tests were ordered by participating HIV clinics (87.6%) with only 3.0% ordered by sexual health/STI/community health clinics and 9.3% by other health providers. Stratum-specific 12-month testing probabilities ranged from 15.8% among sexually inactive men to 42.5% among men reporting 5+ partners (table 2).

At follow-up, 41, 46 and 74 men were diagnosed with chlamydia, gonorrhoea and either pathogen, respectively. The Kaplan–Meier 12-month cumulative incidence proportions were 1.0% (95% CI 0.6% to 1.4%) for chlamydia, 1.2% (95% CI 0.7% to 1.7%) for gonorrhoea and 1.7% (95% CI 1.1% to 2.2%) for the composite outcome. Among cases, 53% (39 of 74) had a history of syphilis compared with 9.5% among non-cases.

Multiple sex partners and recreational drug use were significant risk factors for diagnosis (table 2). Risk was elevated

Table 2 Behavioural risk factors for a diagnosis of genital chlamydia/gonorrhoea infection at follow-up among HIV-positive MSM, OHTN Cohort Study, 2010–2013

Sexual behaviours in preceding 3 months*	Cumulative probability of testing at 12 months (95% CI)†	Cumulative incidence of diagnosis at 12 months (95% CI)†	Unadjusted HR (95% CI)	Multivariable model A‡: adjusted HR (95% CI)	Multivariable model B‡: adjusted HR (95% CI)
Number of sexual partners					
None	15.8 (13.3 to 18.4)	0.4 (0.0 to 0.8)	Reference	Reference	
One	20.0 (16.7 to 23.3)	0.7 (0.0 to 1.4)	2.7 (0.9 to 7.9)		
Two to four	33.9 (29.7 to 38.1)	3.0 (1.5 to 4.6)	10.3 (4.0 to 26.6)	3.1 (1.4 to 6.6)	
Five or more	42.5 (36.7 to 48.3)	4.8 (2.4 to 7.3)	16.0 (6.1 to 41.7)	3.7 (1.7 to 8.3)	
Number of HIV-positive partners					
None	19.0 (16.9 to 21.2)	0.8 (0.3 to 1.2)	Reference		Reference
One	26.8 (22.2 to 31.4)	2.2 (0.7 to 3.8)	2.3 (1.1 to 4.7)		
Two to four	40.1 (34.2 to 45.9)	2.9 (0.9 to 5.0)	5.0 (2.7 to 9.4)		1.6 (0.7 to 3.6)
Five or more	42.3 (32.8 to 51.7)	8.3 (3.1 to 13.5)	13.5 (7.1 to 25.5)		3.3 (1.4 to 7.8)
Number of HIV-negative/status UK partners					
None	20.9 (18.6 to 23.2)	1.1 (0.5 to 1.7)	Reference		Reference
One	22.3 (18.2 to 26.4)	1.0 (0.0 to 2.0)	1.0 (0.5 to 2.0)		
Two to four	34.6 (28.6 to 40.5)	2.5 (0.5 to 4.4)	2.2 (1.2 to 4.3)		1.2 (0.5 to 2.9)
Five or more	33.7 (27.6 to 39.9)	4.8 (2.0 to 7.5)	3.5 (1.9 to 6.2)		1.2 (0.5 to 3.0)
Anal sex					
No partner	15.8 (13.3 to 18.4)	1.0 (0.3 to 1.7)	Reference	Reference	
Sexually active but no anal sex§	20.8 (16.5 to 25.1)	1.3 (0.0 to 2.5)	1.9 (1.1 to 3.3)	0.5 (0.1 to 3.0)	
Anal sex always with a condom	25.6 (21.2 to 30.0)	3.4 (1.5 to 5.3)	1.9 (0.5 to 6.9)	3.3 (1.0 to 11.4)	
Any condomless anal sex	36.8 (32.9, 40.7)	6.0 (4.1 to 8.0)	7.0 (2.5 to 19.0)	3.6 (1.0 to 12.3)	
Anal sex with HIV+ partner					
No HIV+ partner	19.0 (16.9 to 21.2)	0.8 (0.3 to 1.2)	Reference		Reference
Sexually active with HIV+ partner but no anal sex§	17.1 (10.7 to 23.5)	0.0 (0.0 to 0.0)	1.0 (0.2 to 4.4)		1.2 (0.3 to 5.2)
Anal sex with HIV+ partner always with a condom	28.5 (21.5 to 35.4)	1.2 (0.0 to 2.8)	4.0 (1.8 to 8.8)		2.8 (0.6 to 13.4)
Any condomless anal sex with HIV+ partner	40.6 (35.9 to 45.2)	5.4 (3.3 to 7.5)	6.3 (3.7 to 10.8)		2.2 (0.5 to 9.8)
Anal sex with HIV−/UK partner					
No HIV−/UK partner	20.9 (18.6 to 23.2)	1.1 (0.5 to 1.7)	Reference		Reference
Sexually active with HIV−/UK partner but no anal sex§	22.3 (16.9 to 27.7)	0.4 (0.0 to 1.3)	0.7 (0.2 to 2.0)		1.6 (1.5 to 5.1)
Anal sex with HIV−/UK partner always with a condom	29.6 (25.0 to 34.2)	2.8 (1.2 to 4.5)	2.0 (1.1 to 3.7)		2.2 (0.7 to 6.9)
Any condomless anal sex with HIV−/UK partner	35.0 (29.3 to 40.7)	3.3 (1.2 to 5.5)	3.0 (1.6 to 5.3)		1.7 (0.6 to 5.3)
Any recreational drug use in preceding 6 months¶					
No	21.1 (19.2 to 23.0)	0.9 (0.4 to 1.3)	Reference	Reference	Reference
Yes	38.2 (33.7 to 42.8)	4.7 (2.8 to 6.7)	5.0 (3.1 to 5.9)	1.8 (1.1 to 3.2)	2.2 (1.2 to 3.9)

UK=status unknown.
*Behaviours were time-updated at each completion of a sexual behaviour questionnaire.
†Cumulative incidence proportions for testing and diagnosis were calculated using Kaplan–Meier methods.
‡Multivariable models adjusted for variables shown plus baseline age, region and time-updated viral load. Model A includes measures of sexual behaviours with HIV-negative, HIV-positive and HIV status unknown partners grouped together. Model B distinguishes sexual behaviour according to partners' HIV status.
§The category 'sexually active, but no anal sex' was assigned to men who reported one or more partners to the question 'In the last 3 months how many male partners have you had sex with?' but responded 'Never' to the statements 'I had anal sex with him' for any reported HIV-positive or HIV-negative/status unknown partner.
¶Drug use was time -updated at each completion of a face-to-face interview. All drugs were combined to avoid multicollinearity.
MSM, men who have sex with men.

among men who reported 5+ HIV-positive partners but not for multiple HIV-negative/unknown partners in the adjusted model. Recreational drug use doubled risk. Point estimates indicated elevated risk with anal sex (regardless of condom use); however, there was inadequate precision to indicate statistical significance.

DISCUSSION

Among gay and other MSM in an Ontario HIV-positive clinical cohort from 2010 to 2013, the 12-month cumulative incidence of a genital chlamydia/gonorrhoea diagnosis was substantial at 1.7% (95% CI 1.1% to 2.2%). Risk factors were having multiple HIV-positive partners and recreational drug use. Strengths of our analysis include a large sample, tests from a single laboratory and 98% completion rate of the sexual behaviour questionnaire. To our knowledge, our study is the first to compare longitudinal chlamydia/gonorrhoea diagnosis rates from multiple clinics among HIV-positive MSM by partners' HIV status.

There are limitations. Canadian and US guidelines recommend extragenital testing if engaging in oral or rectal intercourse[2] yet such tests were rarely done in our setting, meaning we could not identify rectal or pharyngeal infection risk factors. A 3-month time frame for sexual behaviours mitigated recall error but resulted in unmeasured behaviour between annual questionnaires, potentially explaining the non-zero diagnosis rate among men reporting no partners. Measurement of recreational drug use via face-to-face interviews may have introduced social desirability bias. Voluntary participation may have introduced selection bias. The OCS under-represents recent diagnoses; however, participants are generalisable to HIV-positive persons in Ontario according to sex, region, age at diagnosis and HIV exposure category.[7]

Recreational drug use was also a risk factor for chlamydia/gonorrhoea diagnosis in cross-sectional prevalence studies executed in clinics in Madrid and the Netherlands,[4 5] which was demonstrated for genital, rectal and pharyngeal infections. The Netherlands study reported multiple partners as a risk factor for chlamydia, gonorrhoea and syphilis combined; however, the association became null when syphilis and chlamydia/gonorrhoea were analysed separately. The Madrid study reported risk associated with serosorting, defined as having a stable HIV-positive partner, whereas in our setting having multiple HIV-positive partners was most important.

Only 5% of men reported 5+ HIV-positive partners, but risk was highest in this group, with 12-month diagnosis rates of 8.3% (95% CI 3.1% to 13.5%). After adjustment for HIV-positive partners, no additional risk was associated with having multiple HIV-negative/unknown partners. We propose three hypotheses. First, men may use condoms less frequently for 'poz' sex; however, we observed similar risks between condom users and non-users. Second, HIV-positive men may choose receptive anal sex with HIV-negative partners reducing their risk of genital infection;[3] however, information on seropositioning was unavailable. Third, chlamydia/gonorrhoea may have achieved high prevalence in sexual networks among HIV-positive MSM seeking other positive men, and these networks may have low connectedness with HIV-negative MSM. That half of cases had a history of syphilis suggests presence of a core group where bacterial STIs are concentrated. In a study of German MSM, HIV-positive serosorters had threefold higher odds of bacterial STIs versus those with serodiscordant partners.[8] Together with our finding of heightened risk for recreational drug use, we recommend further investigation of how 'scene' participation (eg, poz parties, bathhouses) influences STI risk.[1] Further, as more HIV-negative men use pre-exposure prophylaxis for HIV prevention, sexual networks between HIV-negative and HIV-positive men may become more connected if serosorting becomes less common,[9] resulting in more population-level transmission of bacterial STI.

Our findings have implications for chlamydia/gonorrhoea prevention, testing and treatment among HIV-positive MSM. Non-zero diagnosis rates among men reporting condom-protected anal sex suggests some acquisition through unmeasured risk practices such as oral sex;[1] sexual education messages should emphasise the differences in bacterial STI transmission routes compared with HIV. Testing was below recommended guidelines; the proportion of untested men reporting high-risk behaviours was substantial. We strongly encourage rectal testing which could detect up to 80% more asymptomatic infections.[5] There is a need to design and deliver interventions to promote safer sex and testing in ways that are engaging, non-stigmatising and acceptable for men at risk. Potential clinic-based interventions to optimise testing include algorithms targeting high-risk patients, clinical decision support systems, automated patient/provider alerts and laboratory technologies to improve case detection.[10]

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Contributors RG conducted the analysis and wrote the manuscript. ANB was the principal investigator who conceived the project, obtained funding and contributed to the direction of the analysis and manuscript writing; she is the guarantor. ANB and SBR directed data collection at clinic sites. VGA and TM directed laboratory analysis at the PHOL and its interpretation. SG, VM and JR provided statistical expertise. AMB, RK, DHST and FM, contributed to the study protocol and guided interpretation. All authors provided critical input into the analysis, read an earlier version of the paper, provided substantive feedback and approved the final paper.

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