Incidence of sexually transmitted infections before and after preexposure prophylaxis for HIV

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Objective: Use of preexposure prophylaxis (PrEP) for HIV raises concerns about sexually transmitted infection (STI) incidence because of decreased condom use among MSM. This study examines whether PrEP is associated with STIs in the 12 months following PrEP prescription relative to the 12 months prior to PrEP and if STI rates are higher among PrEP users relative to individuals receiving postexposure prophylaxis (PEP).

Design: Retrospective cohort study including PrEP users with more than 12 months of follow-up before PrEP prescription and individuals receiving PEP from 2010 to 2015 at Clinique l'Actuel (Montréal, Canada).

Methods: Incidence of chlamydia, gonorrhoea, syphilis and hepatitis C virus over 12 months was compared before and after PrEP; and for PrEP versus PEP users using Poisson models to generate incidence rate ratios (IRRs) with 95% confidence intervals (CIs) and adjusted IRRs (aIRRs) controlling for frequency of STI-screening visits. Models comparing PrEP and PEP users were further adjusted for age and education.

Results: One hundred and nine PrEP and 86 PEP users were included. Increased rates of STIs were observed in the 12 months after PrEP relative to the 12 months prior (IRR: 1.72, CI: 1.22–2.41; aIRR: 1.39, CI 0.98–1.96). PrEP users were also at higher STI risk relative to PEP users (IRR: 2.18, CI: 1.46–3.24; aIRR: 1.76, CI: 1.14–2.71).

Conclusion: Increased rates of STIs among individuals after initiation of PrEP may suggest greater risk behaviours during the first year on PrEP. Further studies are needed to measure long-term trends in STI acquisition following PrEP initiation.

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Introduction

Background and rationale

Preexposure prophylaxis (PrEP) with oral tenofovir disoproxil fumarate and emtricitabine (TDF-FTC or Truvada) has been demonstrated to be highly effective at preventing HIV infection in high-risk MSM in three landmark studies [1–3]. In the United States, the Food and Drug Agency approved the use of PrEP in July 2012 [4] and PrEP is now reimbursed through the Medicaid

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program and the majority of private insurers. PrEP is offered through a patchwork of schemes in the United States, and has been pioneered in a number of clinics in the San Francisco Bay Area [5,6]. PrEP was approved by Health Canada in February 2016 as part of a comprehensive HIV Prevention strategy [7,8]. In Quebec, TDF-FTC has been covered as a general benefit of the provincial healthcare coverage since 2007, without restriction to use as PrEP [9].

Concerns have been raised that PrEP use may be accompanied by the phenomena of risk compensation or behavioural disinhibition, whereby PrEP users' perception of decreased risk of HIV acquisition may lead them to engage in overall riskier sexual practices and increase their chances of acquiring sexually transmitted infections (STIs) [10]. Modifiable behaviours which may impact transmission of STIs include: condom use, number of partners, concurrency or gaps between partners, partner characteristics, and healthcare-seeking behaviours [11]. Additionally, MSM may alter HIV risk mitigation practices while on PrEP by decreasing seroadaptive practices such as seeking a partner of similar perceived serostatus (e.g. serosorting), or the use of strategic positioning whenever engaging in anal sex with a partner of known HIV positive status (seropositioning) [12]. Among PrEP users, high rates of STIs have been reported [13–15], as well as high rates of condomless sex [14], and increasing rates of STIs over time [6]. However, data from the US National HIV Behavioural Surveillance surveys have documented secular trends of decreasing rates of condom use prior to PrEP, with the percentage of men with no condomless anal sex partners decreasing from 61% in 2001, to 54% in 2011 and 40% in 2014 [16].

To our knowledge, no published articles have ascertained increases in the rates of STIs in PrEP users measuring incidence rates of STIs prior to and following the initiation of PrEP. Observation of high or increasing rates of STIs in MSM already on PrEP does not establish PrEP as a cause of increased STIs nor the presumed mechanism of risk compensation whenever there is no baseline level with which to compare. Rather than risk compensation, an alternative hypothesis to explain high rates of STIs observed in some PrEP users is that PrEP does not lead to increases in risky sex, but rather that PrEP brings into care a population of MSM who are already at high risk for HIV and STIs. This alternative hypothesis is suggested by the fact that both the PROUD and IPERGAY studies recruited MSM with a substantially higher HIV incidence during study follow-up than expected. Whereas the expected HIV incidence was estimated to be 2.5–3.0 cases per 100 person-years at risk, the observed seroconversion rate per 100 person-years was 9.0 and 6.6 in the deferred PrEP group of the PROUD study and the placebo group of IPERGAY, respectively [2,3].

If PrEP use increases rates of STIs, this suggests a need to reinforce counselling and STI diagnosis and treatment efforts. This would also suggest that PrEP provides an important public health benefit beyond the immediate prevention of HIV infection because it brings into care high-risk MSM who might not otherwise be seeking care for STIs. Even if PrEP is not associated with an increase in STIs, the benefits of bringing presumably higher risk men into care will have public health benefits in terms of HIV prevention. The public health implications of PrEP are, therefore, significant, but different, depending on which scenario is the case. As a result, we conducted a study to ascertain STI diagnoses in a cohort of MSM prior to and after receiving PrEP as well as in a cohort of postexposure prophylaxis (PEP) patients.

Objectives

In this retrospective cohort study, our key objective was to determine whether prescription of PrEP led to an increase in STIs. We compared the incidence of *Chlamydia trachomatis, Neisseria gonorrhoeae* and new infections with syphilis or hepatitis C virus (HCV) 12 months prior to and 12 months following the prescription of PrEP in a cohort of MSM. We also compared incidence of STIs over 12 months to a control group of MSM prescribed PEP. Additionally, the incidence of HIV seroconversion was measured in both cohort groups.

Methods

Setting

The study was conducted at Montreal's *Clinique médicale l'Actuel*, the leading sexual health provider for Canada's second largest city, which has a metropolitan population slightly over 4 million. The clinic is located at the heart of the city's gay 'Village' and was founded in 1984 specifically to offer sexual health services to MSM. Self-identified gay men continue to constitute the core clientele of the clinic. *L'Actuel* follows a large number of MSM who consult regularly for sexual health and adhere to recommendations for at least annual STI and HIV screening. The clinic began offering PrEP to high-risk MSM in 2011, in response both to promising results that had already begun to emerge and to requests from patients. Messages about PrEP availability were disseminated through gay media and word-of-mouth and the *l'Actuel* website [17]. Our study covers the period from 2010 to 2015. All patients signed an informed consent form authorizing use of anonymized clinical data in epidemiological studies. Ethical approval was obtained from Veritas Institutional Review Board.

Participants

From a cohort of PrEP patients, we selected MSM who had at least 12 months of follow-up prior to and following

PrEP prescription. Data was collected from a baseline PrEP questionnaire including behavioural, clinical, and risk assessments. Individuals were prescribed PrEP if they were at least 18 years old and considered at high risk based on reporting at least one seropositive sexual partner with a detectable viral load, or engaging in condomless anal sex with multiple partners whose HIV status was unknown. PrEP was offered as a once-daily or an intermittent ('on-demand') regimen. After inclusion, baseline visit and questionnaire, visits were scheduled every 3 months, and involved repeat behavioural, risk, adherence and side-effect assessment via questionnaire. Screening was performed at the patients' discretion in the year prior to PrEP and scheduled at 3-month intervals during the year on PrEP.

The PEP group included MSM who were prescribed a 28-day course of PEP and had at least one visit for HIV and STI screening within the year after prescription of PEP. Patients were prescribed PEP based on physicians' evaluation of a high-risk exposure within 72 h of consultation; that is, either condomless sex or condom failure with a known seropositive individual believed to have a detectable viral load or via a contact with substantial risk of HIV transmission, such as an anonymous contact at sauna, backroom, or a 'hook-up' through a mobile app.

Variables

Demographic data was obtained from questionnaires filled out by participants in both PrEP and PEP groups. For all patients, screening visits consisted of a standard set of tests: oral and anal swabs and urine samples were collected to test for *Chlamydia trachomatis*/*Neisseria gonorrhoeae* and blood was drawn to test for HIV, syphilis and hepatitis C virus (HCV). HIV rapid tests were performed in clinic (*INSTI HIV-1/HIV-2 Antibody Test*), and all biological specimens obtained from patients were sent to a nearby hospital laboratory for analysis. The Cobas 4800 real-time polymerase chain reaction (PCR) Assay or the BD ProbeTech PCR Assay was used for *C. trachomatis*/*N. gonorrhoeae* was performed on anal and oral swabs and urine samples. The Cobas 4800 assay has been validated for the detection of extra-genital *C. trachomatis*/*N. gonorrhoeae* [18]. For syphilis, all patients were screened with the standard cascade tests: IgG enzyme-linked immunosorbent assays antibody tests, followed by Rapid Plasma Reagin (RPR) tests and treponemal assays (TP-PA). We defined active Syphilis infections based on either a first-ever positive IgG antibody test, with a documented prior negative IgG test on record and a positive confirmatory TP-PA; or a four-fold increase in RPR titres among individuals with a history of syphilis infection. HCV antibody testing was performed using the Monolisa anti-HCV-Plus assay. HIV antigen–antibody tests were performed for all patients regardless of HIV rapid test results. If either the HIV rapid test or antigen–antibody test was returned positive, a confirmatory western blot was performed.

Laboratory results were transmitted as PDF files to physicians and scanned into the electronic medical record. Laboratory results were also transferred electronically into a database used for research purposes containing only patient identification numbers. STI diagnoses were ascertained for each patient using the research database. Chart review of electronic medical records for each patient allowed us to validate cases reported in the database. The accuracy of electronically ascertained results in the research database was verified by manually comparing database results with those in the patient's chart for over 50% of PrEP patients irrespective of STI results. Once the reliability of the electronically received results was established, only positive STI results in the research database were verified by manually confirming if the result was the same in the patient's chart and that each diagnosis represented an incident case of *N. gonorrhoeae* or *C. trachomatis* and a new infection for syphilis. STI cases diagnosed at the PrEP baseline consultation were counted as cases occurring in the year prior to PrEP. Finally, we collected data on the number of STI screening visits for each participant in the 12 months prior to PrEP and following PrEP or for the 12 months following the PEP episode.

Statistical analysis

Baseline sociodemographic and behavioural variables were compared between groups using Mann–Whitney *U*-tests and chi-square tests. For all patients, we measured the number of anal, oral pharyngeal and/or urethral *C. trachomatis* or *N. gonorrhoeae* diagnoses, infectious syphilis diagnoses and HCV diagnoses in the year following enrolment (start of PrEP or PEP prescription). For PrEP patients, all cases of STIs in the year prior to PrEP were also counted. We calculated the frequency of STIs per 100 person-years for *C. trachomatis*, *N. gonorrhoeae*, syphilis, HCV and overall rates of infection (all sites combined) by dividing the number of infections per stratum by the stratum-specific person-time at risk. The incidence-rate-ratio (relative risk) and 95% confidence intervals (CIs) for STIs in the 12 months following PrEP initiation as compared with the 12 months prior to PrEP was examined in a Poisson regression model [19]. In order to account for potential systematic error because of detection bias, we ran adjusted multivariate Poisson models controlling for the number of screening visits during the pre-PrEP and post-PrEP periods.

We also compared 12-month STI incidence following the date of PrEP prescription versus PEP prescription. For these analyses, we used univariate Poisson regression models and multivariate models adjusted for measured confounders including age, education and frequency of STI screening visits. All analyses were performed using Stata 14.0 (Stata Corp., College Station, Texas, USA).

Results

Table 1 presents the demographic and baseline risk characteristics of MSM patients receiving PrEP ($n = 109$) or PEP ($n = 86$). Median age was 36 and 34 among PrEP and PEP users, respectively. Sociodemographic and behavioural data is most detailed for the PrEP cohort, because of a more detailed study questionnaire used for data collection. 71% of PrEP users and 61% of PEP users attained a university level education. PrEP users were also relatively affluent, with over 50% of patients reporting revenue greater than $55 000 per year. Internet and phone apps were the most popularly reported methods of encountering sexual partners.

In the PrEP group, individuals reported having multiple sexual partners at baseline; on average 1 stable partner and 20 occasional partners within 12 months prior to PrEP initiation. All PrEP users received an initial prescription of daily PrEP. At 12 months, 25% of the PrEP users ($N = 27$) had discontinued PrEP therapy. Among those remaining on PrEP, 6.1% of individuals switched to intermittent ('on-demand') PrEP dosing during the study period.

The counts of STIs and the frequency of STIs per 100 person-years of follow-up are reported by exposure in Table 2. Overall, 83.5 STI cases per 100 person-years were detected during the year following PrEP prescription, as compared with 48.6 cases per 100 person-years in the year prior to PrEP. Among PEP users, 38.4 STI cases per 100 person-years were detected. During the 12 months following PrEP prescription, over half of the cohort remained STI-free, however, 30% of PrEP users contracted one STI, 12% contracted two STIs and 9% contracted three or more STIs. As expected, based on the recommendation for screening visits every 3 months for PrEP patients, we measured a significantly greater frequency of screening visits during the year on PrEP as compared with the year prior (median: five visits versus three visits); and compared with the year following a PEP episode (median: five visits versus three visits).

We found a significant association between prescription of PrEP and counted STI cases in the subsequent year compared with the previous year (Table 3). Following PrEP initiation, a 72% increase was observed overall in STIs (IRR: 1.72, 95% CI 1.22–2.40). By site of infection, the observed increased risk was highest for anal *C. trachomatis* (IRR: 2.13, 95% CI 1.16–3.94). After adjustment for the frequency of screening visits, we continued to observe increased STI incidence after PrEP prescription, however, the effect was inconclusive (aIRR: 1.39, 95% CI 0.98–1.96). Moreover, STI cases were increased in PrEP users relative to controls who were only prescribed PEP during the same time period (Table 4).

Table 1. Demographic and baseline risk factors among preexposure prophylaxis and postexposure prophylaxis users.

Demographics and behavioural variables	PrEP users	PEP users	*P* value[a]
Age (years; median, IQR)	36 (31–44)	34 (28–42)	0.2
Education, *N* (%)			
Primary	1 (1.4)	2 (2.6)	0.643
Secondary	9 (12.5)	13 (16.9)	
College	11 (15.3)	15 (19.5)	
University	51 (70.8)	47 (61)	
Method of meeting partners [b], *N* (%)			
Bar	28 (40.6)	11 (12.8)	< 0.001
Sauna	34 (41.5)	19 (22.1)	0.007
Internet/Apps (e.g. Grindr)	51 (68)	37 (43)	0.001
Via friends/work	32 (46.4)	10 (11.6)	< 0.001
Income, *N* (%)			
<$10 000	3 (3.4)	–	
$10 001–20 000	12 (13.6)	–	
$20 001–35 000	7 (8.0)	–	
$35 001–55 000	17 (19.3)	–	
$55 001–75 000	21 (23.9)	–	
>$75 000	28 (31.8)	–	
Number of sexual partners within 12 months prior to PrEP			
Stable, median (IQR)	1 (1–2)	–	
Casual, median (IQR)	20 (10–40)		
Continuance on PrEP at month 12, *N* (%)	82 (75.23)	–	
Frequency of STI screening visits per 12-month period, median (IQR)	Pre-PrEP, 3 (2–5) Post-PrEP, 5 (4–5)	3 (2–4)	<0.001[c]
Total	109	86	

Valid percentages are shown here, data is missing for education ($n = 46$), income ($n = 122$). IQR, interquartile range; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis.
[a]Calculated using Mann–Whitney *U*-test or Chi-square test.
[b]Categories are not mutually exclusive; for the PrEP group, this refers to general patterns over the past 12 months; for the PEP group, this variable refers to the method of meeting the individual (s) with whom the sexual risk encounter occurred.
[c]Significant difference found in testing frequency before versus after PrEP prescription and for post-PrEP versus PEP.

Table 2. Frequency of sexually transmitted infections among individuals during 12-month periods before preexposure prophylaxis, following preexposure prophylaxis prescription and following postexposure prophylaxis therapy.

	Prior to PrEP ($N = 109$)		Following PrEP start ($N = 109$)		Following PEP episode ($N = 86$)	
Variables	Incident cases	Frequency per 100 person-years	Incident cases	Frequency per 100 person-years	Incident cases	Frequency per 100 person-years
Neisseria gonorrhoeae						
Anal	10	9.17	16	14.68	9	10.47
Oral	12	11.01	13	11.93	13	15.12
Urethral	9	8.26	7	6.42	2	2.33
Any site	23	21.10	31	28.44	22	25.58
Chlamydia trachomatis						
Anal	15	13.76	32	29.36	8	9.30
Oral	3	2.75	3	2.75	1	1.16
Urethral	6	5.50	14	12.84	1	1.16
Any site	21	19.27	44	40.37	8	9.30
Syphilis (new infection)	9	8.26	16	14.68	3	3.49
Hepatitis C virus	0	–	0	–	0	–
Total count of STIs	53	48.62	91	83.5	33	38.4
HIV seroconversion	–		2	1.85 (0.46–7.42)	1	1.16 (0.16–8.23)
Total number of STIs per individual, *N* (%)						
Zero cases	72	66.06%	57	52.29%	60	69.70%
One case	25	22.94%	29	29.61%	19	22.09%
Two cases	8	7.34%	13	11.93%	7	8.14%
At least three cases	4	3.67%	10	9.17%	0	0%

Incidence rate estimated as number of incident STI cases per 100 person-years at risk. PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection.

The 12-month risk of STIs was higher among PrEP patients relative to PEP controls (IRR: 2.18, 95% CI 1.46–3.24; aIRR: 1.76, 95% CI 1.14–2.71).

HIV infections were observed in both groups during the follow-up period (Table 2). Although there were two new HIV infections diagnosed in the PrEP group, chart review demonstrated that neither of these patients were taking PrEP prior to seroconversion. Of the two patients who seroconverted in the PrEP group, one patient tested positive for HIV 3 months after PrEP discontinuation, and the other patient was likely in a seroconversion window period at the time of PrEP prescription as primoinfection symptoms arose shortly after PrEP initiation. In the PEP group, one patient seroconverted 3 months after the successful completion of his 28-day course of PEP.

Table 3. Risk of sexually transmitted infections among preexposure prophylaxis patients in the 12 months following preexposure prophylaxis initiation versus 12 months prior to preexposure prophylaxis.

	IRR	95% CI	aIRR[a]	95% CI
Neisseria gonorrhoeae				
Anal	1.6	0.73–3.53	1.29	0.57–2.89
Oral	1.08	0.49–2.37	0.85	0.38–1.90
Urethral	0.78	0.29–2.09	0.60	0.22–1.64
Any site	1.35	0.79–2.31	1.05	0.60–1.82
Chlamydia trachomatis				
Anal	**2.13**	**1.16–3.94**	1.78	0.95–3.34
Oral	1	0.20–4.96	0.75	0.15–3.81
Urethral	2.33	0.90–6.07	1.85	0.70–4.91
Any site	**2.10**	**1.25–3.52**	**1.74**	**1.02–2.96**
Syphilis	1.78	0.79–4.02	1.47	0.64–3.40
All combined	**1.72**	**1.22–2.41**	1.39	0.98–1.96

aIRRs, adjusted incidence rate ratios; IRRs, incidence rate ratios. Bold values denote statistically significant estimates.
[a]Adjusted IRR controls for the frequency of screening during the 12 months before and after PrEP prescription.

Discussion

Our data supports the hypothesis of risk compensation among patients who initiate PrEP. Greater rates of STIs were observed in the year following PrEP initiation relative to the year prior, indicating that patients may be engaging in higher risk activities for STIs while on PrEP. For *N. gonorrhoeae*, the relative risk was highest with anal and oral cases, though overall not statistically significant. The lower relative risk with urethral *N. gonorrhoeae* is consistent with the fact that urethral *N. gonorrhoeae* is most often symptomatic and patients would have, therefore, been less likely to engage in condomless sex if suffering from dysuria and/or penile discharge. The lower relative risk for urethral infections was not observed for *C. trachomatis*, which is also consistent as higher rates of asymptomatic infections are found with anal and urethral *C. trachomatis* than with *N. gonorrhoeae*, and both oral *C. trachomatis* and *N. gonorrhoeae* are usually not symptomatic. In summary, the highest relative risk was for infections more likely to be asymptomatic, suggesting risk compensation as a possible mechanism.

This data reflects the increased risk of STIs after PrEP initiation among individuals who were already engaged in care at a sexual health clinic. Our PrEP study population likely represents a group of individuals who perceive

Table 4. Risk of sexually transmitted infections in the 12 months following preexposure prophylaxis initiation versus postexposure prophylaxis therapy.

	IRR	95% CI	aIRR[a] model 1	95% CI	aIRR[b] model 2	95% CI
Neisseria gonorrhoeae						
Anal	1.40	0.62–3.17	1.05	0.45–2.48	1.36	0.55–3.37
Oral	0.79	0.37–1.70	0.54	0.24–1.22	0.53	0.23–1.25
Urethral	2.76	0.57–13.29	1.98	0.39–10.09	2.42	0.47–12.55
Any site	1.11	0.64–1.92	0.76	0.42–1.35	0.86	0.47–1.56
Chlamydia trachomatis						
Anal	**3.16**	**1.45–6.85**	**2.75**	**1.24–6.13**	**3.15**	**1.37–7.24**
Oral	2.37	0.25–22.76	1.47	0.14–15.63	2.74	0.22–34.42
Urethral	**11.05**	**1.45–84**	7.59	0.97–59.27	**8.76**	**1.06–72.44**
any site	**4.34**	**2.04–9.22**	**3.61**	**1.67–7.83**	**3.98**	**1.79–8.88**
Syphilis	**4.21**	**1.23–14.44**	3.03	0.85–10.763	2.85	0.76–10.68
All combined	**2.18**	**1.46–3.24**	**1.63**	**1.08–2.47**	**1.76**	**1.14–2.71**

aIRRs, adjusted incidence rate ratios; CI, confidence interval; IRRs, incidence rate ratios. Bold values denote statistically significant estimates.
[a]Model 1 is adjusted for frequency of screening visits only.
[b]Model 2 is adjusted for screening frequency, age and education.

themselves to be at high risk of HIV acquisition and have high levels of health literacy, as shown by both their history of frequent screening in the 12 months prior to PrEP start [20] and their early adoption of PrEP during its period of introduction to Montréal (2011–2015). Notably, in our cohort, we did not observe any HCV infections during the follow-up period; however, two of the participants (one PrEP and one PEP user) had been previously infected and spontaneously cleared HCV. This indicates that HCV rates among MSM in our setting are lower than the reported 4.8% HCV prevalence among MSM in PrEP clinics in Amsterdam [21].

MSM who have been diagnosed with rectal STIs or syphilis have been shown to be at increased risk for HIV [22], therefore, high rates of STIs experienced by the PrEP users in our study provide support and justification for their continuance on this therapy. It is also important that patients who consider discontinuing PrEP receive risk counselling from a trained healthcare professional regarding their HIV risk prior to stopping PrEP. In the 12-month follow-up of PrEP users in our study, we found 25% of individuals discontinued PrEP; regretfully, one of these individuals became subsequently infected with HIV.

Remarkably, the relative risk of STIs was higher for patients on PrEP even compared with patients who had been prescribed PEP and therefore had reported at least one potentially high-risk encounter. There is anecdotal evidence that patients coming for PEP are frequently eligible for PrEP based on ongoing risk level; however, even if this had been the case in our population, PEP patients had lower ongoing STI risk. This lends weight to the hypothesis that PrEP may contribute to risk compensation whereas PEP patients are more likely to represent regular condom users who consult in the event of isolated condom failure incidents.

It is possible that prior to PrEP, individuals engaged in multiple risk-mitigation strategies, including limiting their number of sexual contacts, condom usage, serosorting and seropositioning and once on PrEP, they perceived themselves to be at lower risk and therefore, decreased one or more of their former risk mitigation strategies. Shifts in risk behaviour may bring individuals into contact with individuals who are engaged in large and active sexual networks wherever rates of STI transmission may be higher [23]. Sexual networks, and the behaviours of individuals with high contact rates can affect STI transmission and incidence rates at a population level [24].

STI incidence detected among PrEP users in our study was lower than estimates reported by others [14,15,25]. A meta-analysis summarizing rates of STIs among MSM on PrEP or without PrEP found IRRs of 25.3 for *N. gonorrhoeae* and 11.2 for *C. trachomatis* [25]. However, this meta-analysis used non-PrEP controls from pre-2010 and is, therefore, subject to bias because of secular time trends in STI incidence [26]. The more modest IRRs documented in our study are, thus, less subject to bias because of our use of before/after measures among the same group of PrEP patients or the comparator group of PEP users, who accessed treatment during the same period as the PrEP patients. Our findings are supported by similar results from the PROUD study, which documented ongoing high rates of rectal STIs during the deferred and immediate PrEP phases of the study and increases in rectal *C. trachomatis* whenever individuals in the deferred phase initiated PrEP [27].

Our study has several limitations. Comparison between PrEP and PEP groups is limited by the fact that different questionnaires were used, thus, precluding direct comparisons of sexual behaviour and limiting our ability to control for reported sexual behaviour. Allocation to the comparator PEP group was not randomized, therefore, confounding between groups is possible. Furthermore, despite efforts to control for detection bias because of systematic screening of the PrEP group, it is

possible that bias in detection rates remains. Follow-up behavioural risk data on condom use and changes in number of sexual partners during the study period for the PrEP cohort was largely incomplete, limiting our ability to draw inferences on behaviour changes resulting from PrEP use. It is possible that STIs were detected among study participants outside of the study site and were not reported by participants; however, efforts were made to minimize this possibility by restricting the study to include patients with sufficient follow-up before and after PrEP or PEP. The influence of selection bias and confounding because of secular trends in sexual behaviour or STI incidence from 2010 to 2015 cannot be ruled out. Data from the provincial surveillance, thus, indicated that the incidence of *N. gonorrhoeae* in Quebec increased from 35.0 to 69.4 cases per 100 000 men from 2010 to 2015, respectively. Similarly, for *C. trachomatis* the incidence increased from 137.7 to 218.7 per 100 000 men from 2010 to 2015, respectively [28].

Conclusion

This study evaluated the impact of PrEP on STI in a cohort of MSM before and after initiation of PrEP. In this real-world population, PrEP appears to have been effective based on the fact that no HIV infections occurred among patients who were adherent to PrEP and seronegative at baseline. The increase in STIs was more notable for infections that are usually asymptomatic than for those with florid symptoms, as could be expected since symptoms would drive behavioural changes to reduce transmission (i.e. abstinence or condom use during symptoms). This study suggests that in our population of MSM in a large North American city, PrEP may lead to increased risk of STIs, and that STI prevention, diagnosis and treatment should continue to be offered at quarterly intervals.

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Author contributions: V.K.N. was responsible for study conception and design, literature search, data interpretation and manuscript writing. Z.R.G. was responsible for literature search, data analysis, data interpretation and manuscript writing. H.T. was responsible for study conception and design, data analysis, data interpretation and manuscript writing. M.C., A.G., M.B., L.C., D.L., S.L. and H.G.B. were responsible for data collection and data interpretation, and manuscript review. R.T. was responsible for study design, data collection, data interpretation and manuscript review.

Conflicts of interest

V.K.N. has received speaker's fees from Gilead. H.T. has received grants through her institution from ViiV, Merck and Gilead. R.T. has received grants and personal fees from Gilead, Merck, ViiV and AbbVie.

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