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# Pre-exposure prophylaxis and bacterial sexually transmitted infections (STIs) among gay and bisexual men

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## ABSTRACT

**Objectives** While pre-exposure prophylaxis (PrEP) prevents HIV acquisition among gay, bisexual and other men who have sex with men (GBM), PrEP-using GBM may be more likely to engage in sexual behaviours associated with bacterial STIs. We examined associations between PrEP use, condomless anal sex (CAS), number of anal sex partners, oral sex and bacterial STI diagnoses among GBM living in Canada's three largest cities.

**Methods** Among HIV-negative/unknown-status GBM in the baseline of the Engage cohort study, we fit a structural equation model of the associations between any PrEP use, sexual behaviours and bacterial STI diagnosis. We estimated direct and indirect paths between PrEP use and STI via CAS, number of anal sex partners and oral sex.

**Results** The sample included 2007 HIV-negative/unknown status GBM in Montreal, Toronto and Vancouver. There was a significant direct association between PrEP use and current STI diagnosis (β=0.181; 95% CI: 0.112 to 0.247; p<0.001), CAS (β=0.275; 95% CI: 0.189 to 0.361; p<0.001) and number of anal sex partners (β=0.193; 95% CI: 0.161 to 0.225; p<0.001). In the mediated model, the direct association between PrEP use and STIs was non-significant. However, the indirect paths from PrEP to CAS to STIs (β=0.064; 95% CI: 0.025 to 0.120; p=0.008), and from PrEP to greater number of anal sex partners to CAS to STIs were significant (β=0.059; 95% CI: 0.024 to 0.108; p=0.007).

**Conclusions** Our study adds to the growing awareness that PrEP use among GBM may be associated with bacterial STIs because PrEP users have more anal sex partners and are more likely to engage in CAS. The results underscore the importance of providing effective STI counselling and regular testing to PrEP users, adapting PrEP care and related STI testing to individual needs, and the need for effective prevention strategies for bacterial STIs.

## KEY MESSAGES

⇒ WHAT IS ALREADY KNOWN ON THIS TOPIC:
Both Pre-exposure prophylaxis (PrEP) and bacterial STIs are increasing among gay, bisexual, and other men who have sex with men (GBM).

⇒ WHAT THIS STUDY ADDS:
PrEP was indirectly associated with bacterial STIs via two pathways: through condomless anal sex, and through number of sex partners and condomless anal sex.
PrEP was not directly associated with bacterial STIs when controlling for number of sex partners, oral sex and condomless anal sex among gay, bisexual and other men who have sex with men (GBM).

⇒ HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY: PrEP for bacterial STIs and behavioural STI risk reduction interventions are needed to reduce the burden of bacterial STIs among PrEP-using GBM.

## INTRODUCTION

Gay, bisexual and other men who have sex with men (GBM) continue to be disproportionately affected by HIV. In 2018, GBM accounted for 41.4% of all reported cases among Canadian adults.[1] Significant advances in biomedical methods of HIV prevention have occurred in the past decade; in particular, HIV pre-exposure prophylaxis (PrEP[2]). As optimism about the ability of PrEP to reduce HIV infections among GBM continues to increase,[3] concerns have been raised about how increased PrEP may lead to an increase in STI/HIV risk behaviours occurring as a result of confidence in the protective effects of PrEP against HIV.[4] Indeed, since PrEP received approval in the USA and Canada, there have been increases in bacterial STIs such as syphilis and gonorrhoea among US GBM and in the general population in Canada,[5 6] although these trends were present before PrEP.

A recent systematic review of 13 open-label PrEP trials with mostly GBM samples[7] found that use of PrEP was not associated with presence of any STI, although findings trended toward statistical significance. These findings differ somewhat from a previous meta-analysis, which found that compared with GBM not taking PrEP, PrEP-using GBM were 25.4, 11.2 and 44.6 times more likely to acquire gonorrhoea, chlamydia and syphilis, respectively.[8]

### Pathways by which PrEP may be associated with STIs

Importantly, no studies have examined the pathways by which PrEP could be associated with STIs. The lack of data is problematic as PrEP is unlikely to be directly associated with STIs, and instead may be indirectly associated with STIs via sexual behaviours. Current findings also differ regarding the association between PrEP use and sexual behaviours. In Traeger *et al*,[7] none of the studies reported a statistically significant increase in the proportion of men reporting any condomless anal sex (CAS) from baseline to follow-up. However, in more recent research, PrEP initiation was associated with an increase in the proportion of GBM reporting never using condoms during anal sex as well as increases in the number of CAS partners.[9 10] Other studies indicate that, as PrEP use increases, condom use simultaneously decreases.[11] Although evidence has not been consistent on associations between PrEP and number of male sex partners,[7 11] if PrEP is associated with an increased number of male sex partners, PrEP would also indirectly increase the likelihood of engaging in any sexual behaviour, including CAS and oral sex.

Few studies have examined links between PreP and oral sex despite the demonstrated association between oral sex and STI diagnoses among GBM.[12] Oldenburg *et al*[10] found a non-significant increase in the mean number of oral sex partners after initiating PrEP. These findings are supported by other research showing that pharyngeal gonorrhoea and chlamydia rates remained the same or slightly increased following PrEP initiation.[9]

### Methodological issues in the extant literature

Most studies on PrEP and STIs have focused on clinical samples of men seeking STI treatment or to initiate PrEP.[7–9] GBM who enrol in PrEP studies may have a greater risk of contracting STIs compared with other eligible GBM who do not.[8] Observed increases in STI diagnoses found among sexual health treatment-seeking GBM using PrEP may also reflect the increased STI testing that occurs among GBM taking PrEP as part of routine PrEP care.[9] It is therefore beneficial to explore associations between PrEP and bacterial STIs in a population-based sample of HIV-negative GBM. Most importantly, the literature still lacks data on the pathways by which PrEP may be indirectly associated with STIs via increased sexual behaviours among PrEP-using GBM.

### The present study

To address these gaps in the literature, we examined the direct and indirect associations between PrEP and bacterial STIs in a large three-city, community-based sample of GBM. We hypothesised that (1) PrEP use would be directly associated with bacterial STIs and (2) that PrEP use would be indirectly associated with bacterial STIs via three sexual behaviours among PrEP users in the past 6 months: (a) engaging in CAS, (b) engaging in oral sex and (c) number of sex partners. Third, we hypothesised that PrEP may be associated with STIs via a two-step pathway, by which PrEP use is associated with number of male sex partners, which in turn is associated with both CAS and oral sex. Lastly, we hypothesised that the direct association between PrEP use and bacterial STIs would be attenuated when accounting for the presence of CAS, oral sex and number of anal sex partners in the past 6 months.

## METHODS

### Procedures

Details of the Engage Study sample and methodology have previously been published.[13 14] Engage combines data from computer-assisted self-interviewing and the detection of HIV and other selected STIs and blood-borne infections using biological samples. Participants were recruited using respondent-driven sampling (RDS). RDS is a modified form of chain-referral sampling designed to approximate probabilistic samples by adjusting for selection bias.[15] GBM were eligible to participate in the study if they (1) were aged ≥16 years, (2) self-identified as a man (cisgender or transgender), (3) were able to read English or French, (4) lived in the metropolitan area of the data collection city, (5) had engaged in sexual activity with another man in the 6 months prior to their study visit. After providing written informed consent, seed participants and subsequent participants completed the study questionnaire and biological sampling for sexually transmitted and blood -borne infections (STBBIs) and were briefly educated on how to refer other eligible GBM. Each participant received six vouchers to recruit GBM from their own social or sexual networks. Participants received $C50 compensation for their participation and a secondary incentive of $15 for each eligible GBM they recruited. Each voucher had a unique number to track a participant to his recruiter (thereby establishing recruitment chains and allowing for RDS statistical adjustments) and to facilitate the secondary incentive payment.

### Measures

#### Sociodemographic variables

Participants reported their sociodemographic characteristics including age, ethnocultural background, income, sexual identity, HIV status, relationship status and city.

#### Biological sampling and STBBI testing

At each study site, participants provided a venous blood sample permitting serological testing for HIV, hepatitis C virus, hepatitis B virus and syphilis; these tests were done according to provincial laboratory algorithms, which are similar in the three cities. A history of syphilis infection was based on a positive anti-treponemal antibody test and a rapid plasmin reagin titre ≥1:16. Participants also provided urine, pharyngeal swab, and rectal swabs to screen for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using nucleic acid amplification testing (NAAT) or culture, based on provincial laboratory testing procedures which evolved over time. Any positive result on a urine, pharyngeal or rectal specimen as a detected infection was coded as a detected infection. Details on biological sampling have previously been published.[13 14]

Due to provincial differences, for throat and rectal samples, half of the participants in Toronto had a culture and half had a NAAT; whereas in Montreal and Vancouver, all specimens underwent NAAT. Gonorrhoea and chlamydia rectal results were not available for 20% of Vancouver participants. We compared participants with no missing test result and with at least one missing test result on the primary exploratory variable (ie, PrEP use), and on demographic characteristics, such as age, race/ethnicity, income, marital status, and sexual orientation. Participants with at least one missing test result were more likely to report higher income and to self-identify as non-gay. To account for this variability, we adjusted our analyses for age, race/ethnicity, income, marital status, sexual orientation and city.

Test results were made available by each site's study nurse to participants within 2 weeks after collection. Study staff provided

all participants who newly tested positive for HIV or other STBBIs with linkage to local care and treatment providers. The Vancouver site provided treatment for gonorrhoea, chlamydia and syphilis on-site. Study staff also provided STBBI transmission risk reduction counselling. For this analysis, we coded each bacterial STI (gonorrhoea, chlamydia and syphilis) as no/yes (not detected/detected infection) and calculated a combined 'any STI' variable based on any detected recent infection of gonorrhoea, or chlamydia, or syphilis.

### PrEP use

We measured any PrEP use in the past 6 months if the participant reported being a current user at the time of interview, reported a date of previous PrEP use that was within the past 6 months from the study visit date or reported use of PrEP with a sexual partner within the past 6 months preceding the study visit.

### Sexual behaviours

We examined three sets of sexual behaviours: number of male anal sex partners, engagement in CAS and engagement in oral sex, all in the past 6 months. For the present analysis, number of male anal sexual partners was standardised with a mean=0 and SD=1 for ease of interpretation. CAS was operationalised as the presence of any anal sex without a condom with at least one male partner. Oral sex was operationalised as the presence of any giving or receiving oral sex in the past 6 months.

## Statistical analyses

We carried out this analysis in two steps. First, we examined sociodemographic characteristics, means, SD and normality assumptions of the measures. Descriptive statistics were generated using frequencies/percentages and medians/IQRs where appropriate.

Second, we fit a structural mediation model, with weighted least squares means and variance-adjusted estimator. This model examined the potential pathways between PrEP use, CAS, number of anal sex partners, oral sex and any recent bacterial STI diagnosis (syphilis, gonorrhoea or chlamydia) at the study visit. Our model examined direct associations from PrEP to the three mediating variables: CAS, number of anal sex partners and oral sex. The model also specified effects of mediating variables on STIs. Each of these direct associations was estimated along with three mediated associations. We used the Comparative Fit Index (CFI), the Tucker-Lewis Fit Index (TLI) and Weighted Root Mean Square Residual (WRMR) to evaluate model fit. We report hypothesised standardised indirect path coefficients and errors, and 95% bias-corrected CIs.[16] Indirect effects were deemed to be significant if the 95% bias-corrected CI did not contain zero.

All models were adjusted for age, race/ethnicity, income, marital status, sexual orientation, city and RDS weights. Data management was performed using STATA/SE V.16.1[17] and mediation analyses were conducted in MPlus V.7.4.[18]

## RESULTS

A total of 2449 GBM in Montreal (n=1179), Toronto (n=517) and in Vancouver (n=753) were recruited from February 2017 to August 2019. Among Engage participants across cities (n=2449), 18% self-reported living with HIV. Table 1 summarises the sample characteristics of 2009 participants with HIV-negative/unknown serostatus. Approximately 18.1% of participants reported PrEP use in the past 6 months and 10. 1% were diagnosed with recent bacterial STI at the study visit (5.4% with gonorrhoea, 6.3% with chlamydia and 1.1% with syphilis). It should be noted that these sample percentages are not true point prevalence as we have combined three unequal city samples. We have reported

**Table 1** Baseline characteristics of HIV-negative and HIV-unknown status participants by PrEP use in past 6 months, Engage cohort study (n=2009)

| | Overall | PrEP use in the last 6 months | | |
|---|---|---|---|---|
| **Characteristics** | **n (%)*** | **Yes (%)*** | **No (%)*** | **P value†** |
| | 2009 | 363 (18.1) | 1646 (81.9) | |
| **Recruiting city** | | | | <0.001 |
| Montreal | 968 (48.2) | 124 (34.2) | 844 (51.3) | |
| Toronto | 419 (20.9) | 89 (24.5) | 330 (20.0) | |
| Vancouver | 622 (30.9) | 150 (41.3) | 472 (28.7) | |
| **Race/ethnicity** | | | | 0.675 |
| White | 1404 (69.9) | 257 (70.8) | 1147 (69.7) | |
| Men of colour | 605 (30.1) | 106 (29.2) | 499 (30.3) | |
| **Education** | | | | <0.001 |
| High school or less | 295 (14.8) | 31 (8.5) | 264 (16.1) | |
| Some college | 636 (31.8) | 97 (26.7) | 539 (33.0) | |
| Bachelor's degree and above | 1068 (53.4) | 235 (64.7) | 833 (50.9) | |
| **Income, CAD, last year** | | | | <0.001 |
| Less than $40 000 | 1235 (61.5) | 177 (48.8) | 1058 (64.3) | |
| $40 000–$79 900 | 595 (29.6) | 129 (35.5) | 466 (28.3) | |
| $80 000 or more | 179 (8.9) | 57 (15.7) | 122 (7.4) | |
| **Sexual identity** | | | | <0.001 |
| Gay | 1631 (81.2) | 325 (89.5) | 1306 (79.3) | |
| Bisexual | 140 (7.0) | 13 (3.6) | 127 (7.7) | |
| Other | 238 (11.8) | 25 (6.9) | 213 (13.0) | |
| **Relationship status** | | | | 0.064 |
| Single | 1447 (72.0) | 245 (67.5) | 1202 (73.0) | |
| Married/common-law | 428 (21.3) | 86 (23.7) | 342 (20.8) | |
| Separated/divorced/ widowed | 134 (6.7) | 32 (8.8) | 102 (6.2) | |
| **STI diagnosis (gonorrhoea or chlamydia or syphilis)** | | | | <0.001 |
| Not detected | 1807 (89.9) | 300 (82.6) | 1507 (91.6) | |
| Detected | 202 (10.1) | 63 (17.4) | 139 (8.4) | |
| **STI diagnosis (gonorrhoea)** | | | | 0.001 |
| Not detected | 1544 (94.6) | 266 (90.8) | 1278 (95.4) | |
| Detected | 88 (5.4) | 27 (9.2) | 61 (4.6) | |
| **STI diagnosis (chlamydia)** | | | | <0.001 |
| Not detected | 1530 (93.7) | 258 (88.4) | 1272 (94.8) | |
| Detected | 103 (6.3) | 34 (11.6) | 69 (5.2) | |
| **STI diagnosis (syphilis)** | | | | |
| Not detected | 1988 (98.9) | 358 (98.6) | 1630 (99.0) | 0.492 |
| Detected | 21 (1.1) | 5 (1.4) | 16 (1.0) | |
| **Sexual behaviours, past 6 months** | | | | |
| Condomless anal sex | | | | <0.001 |
| None | 626 (31.2) | 27 (7.4) | 599 (36.4) | |
| Yes, at least once | 1383 (68.8) | 336 (92.6) | 1047 (63.6) | |
| Oral sex | | | | 0.162 |
| No | 55 (2.7) | 6 (1.7) | 49 (3.0) | |
| Yes | 1954 (97.3) | 357 (98.3) | 1597 (97.0) | |
| | **Median/IQR** | | | **P value‡** |
| Number of anal sex partners, last 6 months | 3 (1–8) | 10 (5–24) | 2 (1–5) | <0.001 |
| Age, in years | 31 (26–39) | 33 (28–39) | 30 (26–39) | <0.001 |

True point prevalence is presented in Hart *et al*.[13] Percentages and statistics are crude, not adjusted for RDS weights.
*Column percentages.
†$\chi^2$ or Fisher's exact test.
‡Wilcoxon rank-sum (Mann-Whitney) test.
CAD, Canadian dollar; PrEP, pre-exposure prophylaxis; RDS, respondent-driven sampling.

**Table 2** Bivariate associations of PrEP use, CAS, oral sex (OS) and number of anal sex partners (NSPs) and any recent bacterial STI diagnosis; baseline data, Engage cohort study (n=2009)

| | | Direct effect | | |
|---|---|---|---|---|
| **Predictor** | **Outcome** | **β** | **95% CI** | **P value** |
| PrEP use | STI | 0.14 | 0.03 to 0.24 | 0.01 |
| OS | STI | 0.23 | 0.10 to 0.36 | <0.001 |
| CAS | STI | 0.38 | 0.27 to 0.48 | <0.001 |
| PrEP use | OS | 0.07 | −0.16 to 0.29 | 0.56 |
| NSPs | OS | 0.19 | −0.12 to 0.49 | 0.24 |
| PrEP use | CAS | 0.28 | 0.17 to 0.38 | <0.001 |
| NSPs | CAS | 0.68 | 0.64 to 0.72 | <0.001 |
| PrEP use | NSPs | 0.30 | 0.23 to 0.37 | <0.001 |

The estimated coefficients are standardised coefficients.
CAS, condomless anal sex; PrEP, pre-exposure prophylaxis.

**Table 3** Direct and indirect (mediated) effects of PrEP use on any recent bacterial STI diagnosis via CAS, oral sex (OS) and number of anal sex partners (NSPs); baseline data, Engage cohort study (n=2009)

| **Predictor** | **Outcome** | **β** | **95% CI** | **P value** |
|---|---|---|---|---|
| **Direct effect** | | | | |
| PrEP use | STI | 0.04 | −0.12 to 0.21 | 0.62 |
| OS | STI | 0.50 | 0.21 to 0.79 | 0.001 |
| CAS | STI | 0.22 | 0.07 to 0.37 | 0.003 |
| PrEP use | OS | 0.06 | −0.17 to 0.30 | 0.59 |
| NSPs | OS | 0.001 | −0.15 to 0.15 | 0.98 |
| PrEP use | CAS | 0.12 | 0.01 to 0.23 | 0.03 |
| NSPs | CAS | 0.53 | 0.47 to 0.59 | <0.001 |
| PrEP use | NSPs | 0.30 | 0.24 to 0.35 | <0.001 |
| **Indirect effect** | | | | |
| PrEP use–OS | STI | 0.033 | −0.08 to 0.14 | 0.57 |
| PrEP use–CAS | STI | 0.027 | −0.01 to 0.06 | 0.11 |
| PrEP use–NSPs–OS | STI | 0.000 | −0.02 to 0.02 | 0.98 |
| PrEP use–NSPs–CAS | STI | 0.035 | 0.01 to 0.06 | 0.003 |
| Total effect | | 0.137 | 0.03 to −0.24 | 0.01 |

The estimated coefficients are standardised coefficients.
CAS, condomless anal sex; PrEP, pre-exposure prophylaxis.

the point prevalences by city of both PrEP and bacterial STIs previously.[13] Most participants self-identified as gay (81.2%), white (69.9%), single (72.0%), highly educated (53.4% with a Bachelor's degree and above) and reported an income of less than $C40 000 in the last year (61.5%).

Regarding sexual activity in the past 6 months, 97.3% reported engaging in oral sex, 68.8% reported CAS and the median number of anal sex partners was 3 (IQR: 1–8). The prevalence of CAS (92.6% vs 63.6%; p<0.001) and STIs at study visit (17.4% vs 8.4%; p<0.001) was both much higher among PrEP users relative to men who did not use PrEP in the past 6 months. The prevalence of oral sex did not differ between the two groups.

Table 2 shows the bivariate associations of PrEP use, sexual behaviours and STI after adjusting for age, race/ethnicity, income, marital status, sexual orientation, city and RDS weights. We found a significant association between PrEP use and current STI diagnosis (β=0.14; 95% CI: 0.03 to 0.24; p=0.01), CAS (β=0.38; 95% CI: 0.27 to 0.48; p<0.001) and oral sex with STI diagnosis (β=0.23; 95% CI: 0.10 to 0.36; p<0.001). PrEP use was significantly associated with CAS (β=0.28; 95% CI: 0.17 to 0.38; p<0.001) and number of anal sex partners (β=0.30; 95% CI: 0.23 to 0.37; p<0.001). PrEP use and oral sex were not significantly associated (β=0.07; 95% CI: −0.16 to 0.29; p=0.56).

Table 3 presents estimates of the direct associations of PrEP use and our three sexual behaviours with STIs at study visit and the indirect associations in our mediated model. Figure 1 depicts the structural mediation model of pathways between PrEP use, CAS, number of anal sex partners, oral sex and any recent bacterial STI diagnosis after controlling for age, race/ethnicity, income, marital status, sexual orientation, city and RDS weights. The fit indices for the structural equation model were acceptable (CFI=0.99, TLI=0.85, root mean square error of approximation (RMSEA)=0.04, 90% CI (0.01 to 0.08), WRMR=0.32), suggesting that the model fits the data well. In the mediated model, the association of PrEP use and STIs was not statistically significant (β=0.04; 95% CI: −0.12 to 0.21; p=0.62). The direct paths from (1) PrEP use to CAS, (2) PrEP use to number of anal sex partners, (3) number of anal sex partners to CAS, (4) CAS to STIs, and (5) oral sex to STIs were all significant. We also observed a significant indirect path from PrEP use to number of anal sex partners to CAS to STIs (β=0.04; 95% CI: 0.01 to 0.06; p=0.003).

## DISCUSSION

In this large, multicity, community-recruited sample of GBM, PrEP use was indirectly associated with the presence of diagnosed bacterial STIs via two pathways. In the first pathway, PrEP use was associated with bacterial STI diagnosis via a greater likelihood of engaging in CAS. In the second pathway, PrEP use was indirectly associated with bacterial STI diagnosis via an increased number of male anal sex partners, which, in turn, was associated with engaging in CAS. Although PrEP was associated with STI diagnosis in the simple, non-mediated model, in the mediated model, the direct path was not statistically significant. Our findings extend recent work showing that GBM who initiate PrEP use were significantly more likely to engage in CAS in the subsequent 6 months.[11] Our study also extends previous literature

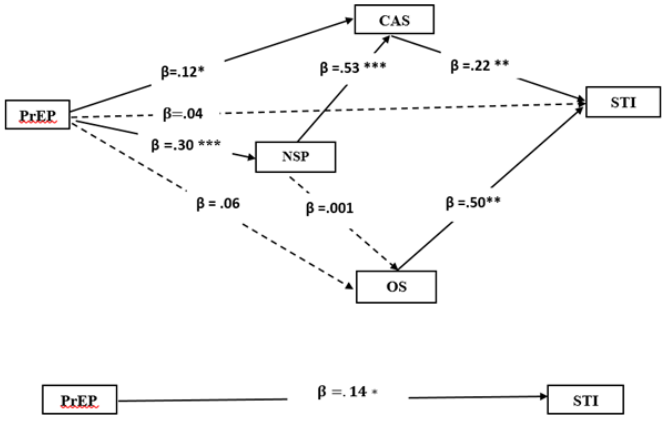


**Figure 1** Associations between pre-exposure prophylaxis (PrEP) use with any recent bacterial STI diagnosis via condomless anal sex (CAS), oral sex (OS) and number of anal sex partners (NSPs). This structural equation model presents associations between PrEP use and bacterial STIs, with intermediary associations of CAS, OS and NSPs. Dotted lines represent non-significant associations; bold lines represent significant indirect paths. β: standardised coefficient; *p<0.05, **p<0.01, ***p<0.001.

focused on clinical cohorts of PrEP users or GBM presenting to STI clinics.[7 8]

Our findings support current recommendations for regular STI testing and risk reduction counselling for GBM who use PrEP.[19 20] It is notable that recent STI diagnoses for GBM who use PrEP were nearly twice that of GBM not using PrEP (19% vs 9%). Public health agencies should therefore consider whether the current standard for frequency of testing for bacterial STIs for PrEP users is sufficient to stem these infections.

### Implications for STI prevention

Our data suggest the need to identify and test STI risk reduction interventions for PrEP users, who are at high risk of STI infection. These interventions will need to address the simultaneous facts that PrEP dramatically reduces the risk of HIV, but that PrEP may still be associated with other STIs via CAS. Several risk factors associated with STIs that may be helpful to consider when designing STI risk reduction interventions for GBM include correcting potentially inaccurate beliefs about STI susceptibility and severity and promoting condom use self-efficacy for PrEP-using GBM who may still occasionally use condoms.[21] Research on PrEP and Post-Exposure Prophylaxis (PEP) for bacterial STIs is also promising[22] and may be increasingly necessary for HIV PrEP users and others at higher risk of bacterial STIs.

As per calls to move beyond 'one-size-fits-all' models of HIV services,[23] these interventions may need to be integrated with social services for PrEP-using GBM who are unstably housed, or with longer term mental health and substance use care. Integrating mental health into STI prevention is consistent with data suggesting the need to address co-occurring psychosocial problems, or syndemic conditions, that disproportionately affect GBM and that are associated with sexual risk behaviours, such as depression, social anxiety and substance use disorders.[24]

### Limitations and future directions

While the current study aimed to recruit a more representative sample of urban GBM,[13 15] our sample has unknown generalisability to GBM in rural areas or smaller cities. Participant self-reports of PrEP and CAS may have also been subject to social desirability biases. The study's focus on structural mediation modelling allowed us to examine bacterial STIs, but power was not sufficient to examine how PrEP may be associated with site of STI or infection with individual STIs. Future studies may also wish to examine differences in PrEP's associations with STIs by type of PrEP regimen (daily or on-demand use), and whether duration of PrEP use is associated with increased or decreased risk of STIs over time.

The cross-sectional nature of the study limits our ability to consider the directionality of findings, as GBM may begin PrEP after contracting a bacterial STI, as recommended in clinical guidelines.[20] Longitudinal studies using community-based recruitment may be able to better discern how increasing PrEP use at the population level predicts increasing STIs, while accounting for other potentially relevant variables.

## CONCLUSION

Our findings provide evidence about number of anal sex partners and CAS as pathways by which PrEP may lead to STIs. This study also extends the literature based on STI cohorts to a large, population-based sample of GBM. Given decreasing use of condoms among GBM and the concurrent rise of STIs, including among PrEP users, there is a need to develop, test and implement additional STI prevention interventions, especially in the context of PrEP, where people may not wish to wear condoms.

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REB#00033527; St Michael's Hospital REB# 17-043; University of Windsor REB# 16-180; University of British Columbia REB# H16-01226) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Participants gave informed consent to participate in the study before taking part.

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## REFERENCES

1 Haddad N, Robert A, Weeks A, *et al*. HIV in Canada—surveillance report, 2018. *Can Commun Dis Rep* 2019;45:304–12.
2 Hull M, Tan DHS. Setting the stage for expanding HIV pre-exposure prophylaxis use in Canada. *Can Commun Dis Rep* 2017;43:272–8.
3 Chen Y-H, Guigayoma J, McFarland W, *et al*. Increases in pre-exposure prophylaxis use and decreases in condom use: behavioral patterns among HIV-negative San Francisco men who have sex with men, 2004–2017. *AIDS Behav* 2019;23:1841–5.
4 Holt M, Lea T, Kippax S, *et al*. Awareness and knowledge of HIV pre-exposure prophylaxis among Australian gay and bisexual men: results of a national, online survey. *Sex Health* 2016;13:359.
5 Mayer KH, Chan PA, R. Patel R, *et al*. Evolving models and ongoing challenges for HIV preexposure prophylaxis implementation in the United States. *J Acquir Immune Defic Syndr* 2018;77:119–27.
6 Public Health Agency of Canada. *Data from: reported cases from 1991 to 2018 in Canada—Notifiable diseases on-line*, 2021. https://diseases.canada.ca/notifiable/charts?c=yl
7 Traeger MW, Schroeder SE, Wright EJ, *et al*. Effects of pre-exposure prophylaxis for the prevention of human immunodeficiency virus infection on sexual risk behavior in men who have sex with men: a systematic review and meta-analysis. *Clin Inf Dis* 2018;67:676–86.
8 Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS* 2016;30:2251–2.
9 Montaño MA, Dombrowski JC, Dasgupta S, *et al*. Changes in sexual behavior and STI diagnoses among MSM initiating PrEP in a clinic setting. *AIDS Behav* 2019;23:548–55.
10 Oldenburg CE, Nunn AS, Montgomery M, *et al*. Behavioral changes following uptake of HIV pre-exposure prophylaxis among men who have sex with men in a clinical setting. *AIDS Behav* 2018;22:1075–9.
11 Bavinton BR, Hammoud MA, Holt M, *et al*. Changes in sexual behaviour following PrEP initiation among Australian gay and bisexual men in relationships: results from a prospective observational study. *AIDS Behav* 2021;25:3704–11.
12 Glynn TR, Operario D, Montgomery M, *et al*. The duality of oral sex for men who have sex with men: an examination into the increase of sexually transmitted infections amid the age of HIV prevention. *AIDS Patient Care STDS* 2017;31:261–7.
13 Hart TA, Moore DM, Noor SW. Prevalence of HIV and sexually transmitted and blood-borne infections, and related preventive and risk behaviours, among gay, bisexual and other men who have sex with men in Montreal, Toronto and Vancouver: results from the engage study. *Can J Pub Health* 2021:1–10.
14 Cox J, Apelian H, Moodie EEM, *et al*. Use of HIV pre-exposure prophylaxis among urban Canadian gay, bisexual and other men who have sex with men: a cross-sectional analysis of the engage cohort study. *CMAJ Open* 2021;9:E529–38.
15 Heckathorn DD. Respondent-driven sampling II: deriving valid population estimates from chain-referral samples of hidden populations. *Soc Probl* 2002;49:11–34.
16 Williams J, Mackinnon DP. Resampling and distribution of the product methods for testing indirect effects in complex models. *Struct Equ Modeling* 2008;15:23–51.
17 STATACorp. *STATA/SE (Version 16.1). [Computer software]*. College Station, TX: StataCorp LLC, 2019.
18 Muthén BO, Muthén LK. *Mplus (Version 7.4) 2015*. Los Angeles, CA, 2015.
19 Centers for Disease Control and Prevention. *US public health service: preexposure prophylaxis for the prevention of HIV infection in the United States—2017 update: a clinical practice guideline*, 2018. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf
20 Tan DHS, Hull MW, Yoong D, *et al*. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *CMAJ* 2017;189:E1448–58.
21 van der Snoek EM, de Wit JBF, Götz HM, *et al*. Incidence of sexually transmitted diseases and HIV infection in men who have sex with men related to knowledge, perceived susceptibility, and perceived severity of sexually transmitted diseases and HIV infection: Dutch MSM-cohort study. *Sex Transm Dis* 2006;33:193–8.
22 Grant JS, Stafylis C, Celum C, *et al*. Doxycycline prophylaxis for bacterial sexually transmitted infections. *Clin Inf Dis* 2020;70:1247–53.
23 Grimsrud A, Bygrave H, Doherty M, *et al*. Reimagining HIV service delivery: the role of differentiated care from prevention to suppression. *J Int AIDS Soc* 2016;19:21484.
24 Stall R, Mills TC, Williamson J, *et al*. Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. *Am J Public Health* 2003;93:939–42.