Original Contribution

Population-Level Sexual Mixing According to HIV Status and Preexposure Prophylaxis Use Among Men Who Have Sex With Men in Montreal, Canada: Implications for HIV Prevention

Linwei Wang, Nasheed Moqueet, Gilles Lambert, Daniel Grace, Ricky Rodrigues, Joseph Cox, Nathan J. Lachowsky, Syed W. Noor, Heather L. Armstrong, Darrell H. S. Tan, Ann N. Burchell, Huiting Ma, Herak Apelian, Jesse Knight, Marc Messier-Peet, Jody Jollimore, Stefan Baral, Trevor A. Hart, David M. Moore, and Sharmistha Mishra*

* Correspondence to Dr. Sharmistha Mishra, MAP Centre for Urban Health Solutions, St. Michael's Hospital, Unity Health Toronto, 209 Victoria Street, Toronto, ON M5B 1T8 (e-mail: sharmistha.mishra@utoronto.ca).

Using cross-sectional survey data (Engage, 2017–2018) from 1,137 men who have sex with men, ≥16 years old, in Montreal, we compared observed human immunodeficiency virus (HIV) seroconcordance in previous-6-months' sexual partnerships with what would have been observed by chance if zero individuals serosorted. Of 5 recent partnerships where both individuals were HIV-negative, we compared observed concordance in preexposure prophylaxis (PrEP) use with the counterfactual if zero individuals selected partners based on PrEP use. We estimated the concordance by chance using a balancing-partnerships approach assuming proportionate mixing. HIV-positive respondents had a higher proportion of HIV-positive partners (66.4%, 95% confidence interval (CI): 64.0, 68.6) than by chance (23.9%, 95% CI: 23.1, 24.7). HIV-negative respondents (both on and not on PrEP) had higher proportions of HIV-negative partners (82.9% (95% CI: 81.1, 84.7) and 90.7% (95% CI: 89.6, 91.7), respectively) compared with by chance (76.1%, 95% CI: 75.3, 76.9); however, those on PrEP had a higher proportion of HIV-positive partners than those not on PrEP (17.1% (95% CI: 15.3, 18.9) vs. 9.3% (95% CI: 8.3, 10.4). Those on PrEP also had a higher proportion of partners on PrEP among their HIV-negative partners (50.6%, 95% CI: 42.5, 58.8) than by chance (28.5%, 95% CI: 27.5, 29.4). The relationship between PrEP and sexual-mixing patterns demonstrated by less population-level serosorting among those on PrEP and PrEP-matching warrants consideration during PrEP roll-out.

HIV; MSM; PrEP; PrEP-matching; serosorting; sexual mixing patterns

Gay, bisexual, and other men who have sex with men (MSM) are disproportionately at risk of human immunodeficiency virus (HIV) acquisition (1). In several epidemic contexts, including in Canada, seroadaptive practices are adopted by some MSM as a strategy to reduce HIV risk (2–6). Seroadaptive practices consider one's own and a partner's HIV status in deciding with whom to have sex, such as choosing sexual partners of the same HIV status (individual-level serosorting), alongside sexual positioning and/or condom use (2–6).

With the scale-up of HIV preexposure prophylaxis (PrEP) and antiretroviral treatment for HIV-positive individuals leading to viral suppression, serosorting, and related patterns of "who has sex with whom" might be changing (7–9). Qualitative evidence suggests that PrEP might reduce stigma and anxiety around sex within serodiscordant partnerships and lead to less serosorting (10). Conversely, PrEP use could be associated with increased stigma if those on PrEP are perceived to have multiple sexual partners, and/or by equating PrEP use with condomless anal sex, thus leading

to preferential partner selection by PrEP use (10). There is also emerging evidence of "biomed-matching," which refers to preferentially selecting sexual partners who are using the same biomedical prevention strategy as oneself, such as individual-level PrEP-matching wherein both partners are using PrEP (7, 9).

Preferential partner selection by any attribute at the individual level can influence the population-level sexual mixing patterns, which in turn influence HIV transmission (11, 12). Individual-level serosorting might be most effective among partnerships in which both partners are certain about HIV status. Individuals might be unaware/uncertain about their own and/or partners' HIV status, thus limiting serosorting effectiveness (13). At the population level, individuals' serosorting might result in fewer serodiscordant partnerships. For instance, in settings with low levels of undiagnosed HIV, this could mean fewer onward HIV transmissions in the context of condomless sex within seroconcordant partnerships (11). Consequently, population-level mixing patterns can further influence the impact of HIV-prevention strategies at the population level (14). Moqueet et al. (14) found that assumptions of no serosorting could underestimate the population-level impact of PrEP on HIV incidence reduction compared with incorporating serosorting in the HIV transmission model.

Despite compelling evidence of individual-level serosorting, there is no empirical estimate that quantifies population-level sexual mixing by HIV status or its relationship with PrEP use. In existing studies, individual-level serosorting was often measured by examining the proportions of MSM who had only seroconcordant partners or who intended to serosort (2–5, 15–24). In a few studies, investigators measured the proportion of seroconcordant partnerships in the sexual network (5, 19, 23). However, to quantify the extent to which the observed partnership distribution reflects preferential partner selection, the observed patterns must be compared with what would have been observed in the absence of individuals' preferential mixing—by chance alone (25).

Using cross-sectional survey data of MSM in Montreal, Canada, we aimed to 1) quantify population-level serosorting by comparing observed partnership distribution by HIV status with that expected by chance; 2) quantify population-level serosorting among HIV-negative MSM stratified by PrEP use; and 3) quantify population-level PrEP-matching by comparing observed partnership distribution by PrEP use with that expected by chance.

METHODS

Study design and subjects

We obtained data (February 7, 2017, to June 15, 2018 (n = 1,179)) from Engage-Montreal, a cross-sectional survey of MSM in Montreal. Cisgender and transgender men aged ≥16 years who had had sex with another man in the previous 6 months were recruited using respondent-driven sampling (RDS) (26, 27). RDS is an adapted form of the chain referral method of recruiting study participants (26, 27). Details on the recruitment procedures for Engage-Montreal

have been documented elsewhere (28). Participants completed a computer-assisted self-interview, which included questions on sexual behaviors in the previous 6 months. We included respondents in our analyses who reported at least 1 anal or oral male sex partner in the previous 6 months, and we excluded respondents who had only vaginal/frontal sex with another man in the previous 6 months (n = 4). We excluded respondents who did not report (different from reporting "unaware") HIV status for all of their sexual partners (n = 38).

Measures

In keeping with terminology for social/sexual-network data, we hereafter refer to respondents as egos and to their sexual partners as alters (29). Ego HIV status was determined by self-report of their most recent HIV test results prior to the current study, and it was classified as positive, negative, or unknown (never tested, did not receive or were unsure about results, or preferred not answering).

Alter HIV status was classified based on ego responses to two sets of questions (Web Appendix 1, available at https://academic.oup.com/aje). One question asked about the aggregate numbers of anal or oral sex partners in the previous 6 months according to alter HIV status (e.g., "of the men you had oral or anal sex with in the past 6 months, how many were HIV-positive?"), which did not separate anal sex from oral sex partners. Responses to these questions were used for our primary analyses on all anal or oral sex partners in the previous 6 months. The other event-level questions (Web Appendix 1) asked about each of up to 5 most recent male sexual partners in the previous 6 months (e.g., "the most recent time you had sex with the partner named above, did you know what his HIV status was BEFORE you guys had sex?"). Respondents could select whether they were certain about their answers (frequency of each response is shown in Web Appendix 2 (Web Tables 1 and 2). We classified uncertain as unknown, to be consistent with the set of questions on the partnerships in the previous 6 months (Web Appendix 1). Event-level questions were asked to distinguish the type of sex (anal, oral, or both) within each partnership (Web Appendix 1). For each ego, event-level data were aggregated to derive total numbers of recent anal or oral sex partners according to alter HIV status, and separately for recent anal sex partners. These event-level measures were used in our sensitivity analyses.

HIV-negative egos' PrEP use in the previous 6 months (yes/no) was ascertained based on self-report of PrEP use anytime in the previous 6 months. We also used event-level data to determine PrEP use at most recent sex (yes/no/unknown) for both egos and alters (e.g., "the most recent time you had sex with the partner named above, were you using PrEP? Was your partner using PrEP?") (Web Appendix 1).

Statistical analysis

We described sociodemographic, sexual behavioral, and health-system engagement characteristics of our study sample. We calculated RDS-adjusted estimates with 95%

empirical likelihood-based confidence intervals, using the Volz and Heckathorn method (RDS-II estimates, calculated using the R (R Foundation for Statistical Computing, Vienna, Austria) "RDS" package), by which individuals were weighted by the inverse of their self-reported network size (survey question in Web Appendix 1) (30).

Analysis: serosorting.   We first estimated the distribution of partnerships according to alter HIV status by chance alone if zero individuals serosort (Web Appendix 3 (equation 1)). This counterfactual cannot be observed, and it was instead estimated under the proportionate-mixing assumption using a balancing-partnerships approach commonly used in mathematical models of HIV (25). Proportionate mixing assumes that by chance alone, the distribution of partnerships "available" by a given attribute depends on the prevalence of this attribute and the heterogeneity in partner numbers by this attribute (25). We then calculated the partnership distribution according to alter HIV status by chance conditional on knowing the alter's HIV status.

We calculated the observed previous-6-month partnership distributions according to alter HIV status for egos with HIV-positive, -negative, and unknown status separately, using equation 2 in Web Appendix 3. The observed partnership distributions according to alter HIV status conditional on knowing the alter's HIV status were also calculated among the subset of alters whose HIV status were known.

We compared the observed partnership distributions conditional on knowing the alter's HIV status with those expected by chance, using χ^2 tests, for egos with HIV-positive, -negative, and unknown status, separately. To quantify the extent of serosorting, we calculated the excess fraction of seroconcordance beyond chance by subtracting the seroconcordance by chance from the observed seroconcordance and then dividing by the observed seroconcordance.

Analysis: serosorting stratified by PrEP use.   We calculated the observed partnership distributions according to alter HIV status for HIV-negative egos using equation 2 in Web Appendix 3, stratified by the ego's previous-6-month PrEP use. For HIV-negative egos on PrEP, and those not on PrEP, we compared their observed partnership distributions according to alter HIV status with each other, and separately, to the partnership distribution according to alter HIV status by chance, using χ^2 tests.

Analysis: PrEP-matching.   We first estimated the distribution of HIV-negative partnerships according to alter PrEP use under proportionate-mixing assumption, using equation 3 in Web Appendix 3 (based on egos' previous-6-month PrEP use data). We then calculated the observed partnership distributions according to alter PrEP use using event-level data, stratified by the ego's PrEP use, reflecting PrEP use at last sex within recent anal or oral sex partnerships, in which both partners were HIV-negative (Web Appendix 3 (Equation 4)). The observed partnership distributions according to alter PrEP use conditional on knowing the alter's PrEP use were also calculated by restricting equation 4 in Web Appendix 3 to the subset of alters whose PrEP use was known.

We compared the observed partnership distributions conditional on knowing the alter's PrEP use with those expected by chance, using χ^2 tests, separately, for HIV-negative egos who used PrEP at last sex and those who did not. Finally, we calculated the excess fraction of concordance in PrEP use beyond by chance.

Sensitivity analyses

Although there are established adjustment methods for RDS sampling to generate population-representative individual-level estimates, (30) it is unknown how RDS sampling would influence population-level sexual mixing estimates. Thus, to examine the sensitivity of our results to the sampling strategy, we repeated our analyses using an RDS-weighted sample (size equivalent to the original sample). We computed RDS weights using the Volz and Heckathorn method (30).

To assess the sensitivity of our results to the differences in how event-level and previous-6-month data were recalled and reported, and to the inclusion of oral sex–only partners, we repeated analyses of aims 1 and 2 using event-level data on recent anal or oral sex partners, and separately for recent anal sex partners only to generate the observed partnership distributions according to alter HIV status. We also repeated the aim-2 analyses, stratifying by ego PrEP use at last sex, instead of in the previous 6 months. Finally, we repeated the aim-3 analysis restricting to recent anal sex partners.

We used R, version 3.5.1 (R Foundation for Statistical Computing), for analyses and calculated confidence intervals assuming binomial distributions. All statistical significance tests were 2-sided.

Ethics

The ethics boards at the following institutions approved the study: Ryerson University, St. Michael's Hospital, University of Toronto, University of Windsor, University of British Columbia, University of Victoria, the Simon Fraser University, and the Research Institute of the McGill University Health Centre.

RESULTS

Table 1 shows RDS-adjusted estimates of the study sample characteristics. A total of 1,137 respondents were included for analyses. Their median age was 34 years (interquartile range, 27–49 years). The majority of respondents self-identified as gay (81.5%). Over a third (38.0%) self-identified as "non-French/English Canadian" and 0.9% as "aboriginal or indigenous." Overall, 207 (18.2%) self-reported as HIV-positive, 831 (73.1%) as HIV-negative, and 99 (8.7%) as of unknown status. Respectively, they reported a median of 5 (interquartile range, 3–15), 5 (interquartile range, 3–10), and 3 (interquartile range, 2–6) anal or oral sex partners in the previous 6 months ($P < 0.001$). The majority of HIV-positive respondents reported currently using antiretroviral therapy ($n = 190$ (96.4%)), of whom 174 (91.6%) were virally suppressed. A total of 112 HIV-

Table 1. Crude and Respondent Driven Sampling–Adjusted Estimates of Characteristics of Gay, Bisexual, and Other Men Who Have Sex With Men in the Engage-Montreal Study (*n* = 1,131), Canada, 2017–2018

Characteristic	No. of Respondents	Crude %	RDS-Adjusted[a]	
			%	95% CI
Age, years		34 (27, 49)[b]	37.9 (36.6, 39.2)[c]	
Non-French/English Canadian	427	38.0	46.4	41.2, 51.6
Aboriginal or indigenous	10	0.9	1.2	0.0, 2.6
Sexual orientation				
Bisexual	91	8.0	12.6	9.1, 16.0
Gay	927	81.5	77.0	72.4, 81.5
Straight	5	0.4	1.7	0.0, 4.1
Other[d]	114	10.0	8.7	5.8, 11.6
Single	820	72.1	73.7	69.1, 78.4
Has a main partner[e]	492	43.3	44.7	39.6, 49.9
Completed university or higher degree	738	64.9	58.8	53.8, 63.7
Employed	767	67.5	56.2	51.1, 61.3
Annual income, Canadian $				
0–9,999	168	14.8	23.4	18.6, 28.1
10,000–29,999	482	42.4	42.4	37.3, 47.5
30,000–69,999	353	31.2	26.1	21.9, 30.3
≥60,000	134	11.8	8.1	5.5, 10.7
No. of anal/oral sex partners, previous 6 months		5 (3, 10)[b]	7.2 (5.4, 8.9)[c]	
Anal sex partners, previous 6 months		3 (1,7)[b]	4.9 (3.2, 6.7)[c]	
Self-reported HIV status[f]				
Negative	831	73.1	73.4	68.9, 77.8
Positive	207	18.2	13.9	10.5, 17.3
Unknown	99	8.7	12.8	9.4, 16.1
Tested HIV positive by the Engage study	208	18.5	14.0	10.5, 17.5
Used PrEP, in previous 6 months[g]	112	13.5	8.9	5.2, 12.6
Currently on ART[h]	190	96.4	97.7	95.2, 100
Virally suppressed[i]	174	91.6	89.7	81.9, 97.3

  Abbreviations: ART: antiretroviral therapy; CI, confidence interval; HIV, human immunodeficiency virus; PrEP, preexposure prophylaxis; RDS, respondent-driven sampling.

  [a] RDS-II estimator and empirical likelihood-based confidence intervals calculated using R (R Foundation for Statistical Computing) "RDS" package.

  [b] Values are expressed as median (interquartile range).

  [c] Values are expressed as RDS-adjusted mean and 95% empirical likelihood-based confidence interval.

  [d] Such as queer, questioning, asexual, pansexual, two-spirit, or other.

  [e] Person with whom the respondent is in a relationship and feels most committed to (even if in a polyamorous, open, or nonmonogamous relationship).

  [f] Self-report of the most recent HIV test results, where unknown was defined as those who never tested for HIV, ever tested but never received the most recent test results, or were unsure or preferred not to answer.

  [g] Among self-reported HIV-negative individuals.

  [h] Among self-reported HIV-positive individuals.

  [i] Among individuals who self-reported being currently on ART.

negative respondents (13.5%) reported using PrEP in the previous 6 months.

Population-level serosorting

Respondents reported information on 11,883 anal or oral sex partnerships in the previous 6 months (Table 2). By chance, the partnership distributions with alters of HIV-negative, -positive, and unknown status were 72.1%, 22.7%, and 5.2%, respectively. However, 43.7% of observed partnerships comprised alters of unknown status. Conditional on knowing alter HIV status, the partnership distributions by chance with alters of HIV-negative and HIV-positive status were 76.1% and 23.9%, respectively (Table 2). HIV-positive egos had a higher proportion of HIV-positive alters than would be expected by chance (66.4% vs. 23.9%; $P < 0.001$) (Table 2). HIV-negative egos and egos with unknown HIV status both had higher proportions of alters with HIV-negative status than would be expected by chance (87.9% and 92.7%, respectively, vs. 76.1%; P for both < 0.001) (Table 2). The excess fractions of HIV-positive seroconcordance and HIV-negative seroconcordance beyond by chance were 64.0% and 13.4%, respectively.

Population-level serosorting stratified by PrEP use

Among HIV-negative egos, those who used PrEP in the previous 6 months had a lower proportion of alters whose HIV status was unknown to egos, compared with those who did not use PrEP (30.6% vs. 49.5%; $P < 0.001$) (Table 3). Conditional on knowing alters' HIV status, HIV-negative egos who used PrEP and those who did not both had lower proportions of HIV-positive alters than would be expected by chance (17.1% and 9.3%, respectively, vs. 23.9%; $P < 0.001$); however, the proportion of HIV-positive alters was higher among those who used PrEP compared with those who did not (17.1% vs. 9.3%; $P < 0.001$) (Table 3). The excess fractions of HIV-negative seroconcordance beyond chance were 8.9% and 16.1% for HIV-negative egos on and not on PrEP, respectively.

Population-level PrEP-matching

HIV-negative respondents reported information on 1,312 recent anal or oral sex partnerships with another HIV-negative man (Table 4). By chance, the partnership distributions with HIV-negative alters who used PrEP and those did not use PrEP were 28.5% and 71.5%, respectively (Table 4). However, in 10.1% of observed recent HIV-negative partnerships, HIV-negative egos did not know alters' PrEP use status. Conditional on knowing alters' PrEP use status, HIV-negative egos on PrEP had a higher proportion of HIV-negative alters who used PrEP at last sex compared with by chance (50.6% vs. 28.5%; $P < 0.001$). Those not on PrEP had a higher proportion of HIV-negative alters who did not use PrEP, compared with what would be expected by chance (80.3% vs. 71.5%; $P < 0.001$) (Table 4). The excess fractions beyond chance of concordance in PrEP use and in no PrEP use were 43.7% and 11.0%, respectively.

Sensitivity analyses

RDS-weighted analyses produced results similar to those of the unweighted analyses. The RDS-weighted proportion of HIV-negative alters, conditional on knowing alters' HIV status, was 81.5% by chance (Web Appendix 4, Web Table 3) and slightly higher than the unweighted estimate (76.1%). The observed proportions of HIV-negative alters were also higher across all subgroups after adjusting for weights (Web Appendix 4, Web Tables 3 and 4). Thus, the RDS-adjusted excess fractions (vs. unweighted) of seroconcordance beyond by chance were 69.9% (vs. 64.0%), 8.4% (vs. 8.9%), and 10.7% (vs. 16.1%) for individuals who were HIV-positive, HIV-negative on PrEP, and HIV-negative not on PrEP, respectively. The RDS-adjusted excess fraction (vs. unweighted) of concordance in PrEP use beyond chance was 42.1% (Web Appendix 4, Web Table 5) (vs. 43.7%). Our results were not sensitive to differences in event-level and previous-6-month data, or to the inclusion of oral sex partners (Web Appendix 5, Web Tables 6–8).

DISCUSSION

We found evidence of population-level serosorting among HIV-positive and HIV-negative MSM in Montreal, Canada, including those who used PrEP. However, there was less serosorting among HIV-negative MSM who used PrEP than among those who did not. We also found evidence of population-level PrEP-matching among HIV-negative MSM. Our empirical estimates of population-level serosorting and PrEP-matching could help in the study of HIV transmission dynamics and in the population-level evaluation of combination HIV-prevention strategies that use HIV transmission models (11, 12, 14, 31).

Our findings of population-level serosorting are consistent with prior studies, which demonstrated serosorting intention or behaviors among MSM in high-income settings (2–4, 6, 15–18, 20, 21, 23, 24). Our population-level measures complement individual-level measures of sexual mixing by addressing the limitations of measuring individuals' intention to preferentially select partners, a measure shown to have low agreement with individual behaviors (20, 23, 24), or measuring individuals' sexual partnering behaviors, which does not distinguish intended behaviors from what could be unintentional (by chance) (2, 3, 15–18, 21). Additionally, our estimates of excess fractions of concordance allowed us to quantify the extent of serosorting and PrEP-matching attributable to individuals' preference beyond by chance. Specifically, a strength of our analyses is that we estimated the partnership distribution by chance under a proportionate-mixing assumption (25), which accounted for the heterogeneity in sexual partner numbers according to HIV status and PrEP use (22).

We found less population-level serosorting among those who used PrEP. This finding aligns with individual-level measure data in Canada, which found that MSM on PrEP reported a higher proportion of HIV-diagnosed partners after starting PrEP (32). Moreover, we found evidence of population-level PrEP-matching, suggesting potential partner preference by PrEP use. Similarly, Grov et al. (7)

Table 2. Seroconcordance Among Anal or Oral Sex Partnerships in the Previous 6 Months as Expected by Chance Under Proportionate Mixing Versus Observed Patterns (Respondents = 1,137; Partnerships Reported by Respondents = 11,883) in the Engage-Montreal Study, Canada, 2017–2018

Respondent HIV Status[a]	No. of Respondents	No. of Respondent-Reported Partnerships	Sexual Mixing Pattern	Sexual Partner HIV Status as Perceived by Respondent						
				Unaware/Unsure		Conditional on Awareness of Sexual Partner HIV status				
						Negative		Positive		
				%	95% CI	%	95% CI	%	95% CI	P Value[b]
N/A	N/A	N/A	Chance[c]	5.2	4.8, 5.6	76.1	75.3, 76.9	23.9	23.1, 24.7	Referent
Negative	831	8,573	Observed	44.2	43.1, 45.2	87.9	87.0, 88.8	12.1	11.2, 13.0	<0.001
Positive	207	2,695	Observed	39.1	37.3, 41.0	33.6	31.4, 36.0	66.4	64.0, 68.6	<0.001
Unknown	99	615	Observed	57.9	53.9, 61.8	92.7	88.8, 95.5	7.3	4.5, 11.2	<0.001

Abbreviations: CI: confidence interval; HIV, human immunodeficiency virus; N/A, not applicable.

[a] Self-report of the most recent HIV test results; unknown was defined as those who never tested for HIV, ever tested but never received the most recent test results, or were unsure or preferred not to answer.

[b] Three χ² tests were performed independently, stratified by respondent HIV status, to compare observed seroconcordance with expected seroconcordance, conditional on respondent awareness of sexual partner HIV status.

[c] Reflects the "total number of anal or oral sex partnerships available by HIV status" under proportionate-mixing assumption, which accounts for the number of individuals by HIV status and different numbers of sexual partners they have.

Table 3. Variability in Seroconcordance Among Anal or Oral Sex Partnerships in the Previous 6 Months by Whether or Not a Self-Reported Seronegative Respondent Used Preexposure Prophylaxis in the Previous 6 Months (Self-Reported Seronegative Respondents = 831; Partnerships Reported by Self-Reported Seronegative Respondents = 8,573) in the Engage-Montreal Study (n = 1,131), Canada, 2017–2018

Respondent PrEP Use, Previous 6 Months[a]	No. of Self-Reported HIV-Negative Respondents	No. of Respondent-Reported Partnerships	Sexual Mixing Pattern	Sexual Partner HIV Status as Perceived by Respondent							
				Unaware/Unsure		Conditional on Awareness of Sexual Partner HIV Status					
						Negative		Positive			
				%	95% CI	%	95% CI	%	95% CI	P Value[b]	P Value[c]
N/A	N/A	N/A	Chance[d]	5.2	4.8, 5.6	76.1	75.3, 76.9	23.9	23.1, 24.7	Referent	N/A
No	719	6,132	Observed	49.5	48.3, 50.8	90.7	89.6, 91.7	9.3	8.3, 10.4	<0.001	Referent
Yes	112	2,441	Observed	30.6	28.8, 32.5	82.9	81.1, 84.7	17.1	15.3, 18.9	<0.001	<0.001

Abbreviations: CI: confidence interval; HIV, human immunodeficiency virus; N/A, not applicable; PrEP: preexposure prophylaxis.

[a] Based on whether the self-reported date of PrEP use at the most recent time was within the previous 6 months.

[b] Two χ^2 tests were performed independently stratified by respondent's PrEP use to compare observed seroconcordance with expected seroconcordance, conditional on awareness of sexual partner HIV status.

[c] A χ^2 test was performed to compare the difference in the two observed seroconcordance by PrEP use conditional on awareness of sexual partner HIV status.

[d] Reflects the "total number of anal or oral sex partnerships available by HIV status" under proportionate-mixing assumption, which accounts for the number of individuals by HIV status and different numbers of sexual partners they have.

Table 4.   Concordance in Preexposure Prophylaxis Use Between Self-Reported Seronegative Respondents and Perceived Seronegative Sexual Partners as Expected With Proportionate Mixing Versus Observed Patterns Among Recent Sexual Partnerships (Self-Reported Seronegative Respondents = 859; Perceived Seronegative Recent Anal or Oral Sex Partners Reported by Self-Reported Seronegative Respondents = 1,312) in the Engage-Montreal Study, Canada, 2017–2018

PrEP, Last Sex[a]	No. of Self-Reported HIV-Negative Respondents	No. of Perceived HIV-Negative Recent Anal or Oral Sexual Partnerships	Sexual Mixing Pattern	Sexual Partner PrEP Use, Last Sex, as Perceived by Respondents							
				Unaware/Unsure		Conditional on Awareness of Sexual Partner PrEP Use					
						No		P Value[b]	Yes		P Value[c]
				%	95% CI	%	95% CI		%	95% CI	
N/A	N/A	N/A	Chance[d]	0.0	0.0, 0.0	71.5	70.6, 72.5	Referent	28.5	27.5, 29.4	N/A
No	765	1,136	Observed	9.8	8.1, 11.6	80.3	77.7, 82.7	<0.001	19.7	17.3, 22.3	Referent
Yes	94	176	Observed	12.5	8.0, 18.3	49.4	41.2, 57.5	<0.001	50.6	42.5, 58.8	<0.001

Abbreviations: CI: confidence interval; HIV, human immunodeficiency virus; N/A, not applicable; PrEP: preexposure prophylaxis.

[a] Self-reported PrEP use at the time of the most recent sex with each partner.

[b] Two χ^2 tests were performed independently to compare observed concordance in PrEP use with expected concordance, conditional on awareness of sexual partner PrEP use.

[c] A χ^2 test was performed to compare the difference in the proportions of partners who use PrEP by respondent's PrEP use conditional on awareness of sexual partner PrEP use status.

[d] Reflects the "total number of HIV-negative anal or oral sexual partnerships available by PrEP use" under proportionate-mixing assumption, which accounts for the number of individuals by PrEP use and different numbers of sexual partners they have.

found that, compared with HIV-negative MSM not on PrEP, those on PrEP reported a larger proportion of partners on PrEP and a smaller proportion of partners not on PrEP (41% vs. 22% and 28% vs. 44%, respectively). Martinez and Jonas (8) found that HIV-negative MSM on PrEP expressed preference toward PrEP users over non-PrEP users while looking for sexual partners online. Nevertheless, we cannot deduce that PrEP use was a causal factor in partner selection, because PrEP-matching could also reflect preferential partner selection by other factors that are associated with PrEP use (e.g., health literacy, HIV risk behaviors, insurance status) (33, 34).

We found that at the population level, awareness of partners' HIV status was higher among MSM who used PrEP than among those who did not. This finding is in contrast with some qualitative evidence that suggests that individuals were less likely to discuss HIV status with partners after initiating PrEP (10). However, our results might reflect an early-adopter effect in our sample. Because PrEP scale-up began in Montreal in 2016 following the approval of emtricitabine/tenofovir disoproxil fumarate (Truvada; Gilead Sciences, Inc., Foster City, California) as PrEP by Health Canada, MSM who used PrEP in our study represent early adopters of PrEP, who might have been more empowered around discussion of HIV status, potentially through prior engagement with HIV-prevention services and strategies (33). With PrEP roll-out, the patterns of population-level sexual mixing are likely to be evolving over time and warrant monitoring, as communities reassemble biomedical evidence and apply it to HIV risk management (35).

Population-level patterns of PrEP-matching and less serosorting while on PrEP could potentially lead to disparities in HIV-prevention benefits between HIV-negative MSM who use PrEP and those who do not; MSM not on PrEP do not directly benefit from the decreased HIV-acquisition risk through taking PrEP, and they might be less likely to benefit from partners' PrEP use if they are less likely to have a partner on PrEP due to population-level PrEP-matching. Moreover, their sexual network reflects a greater extent of serosorting than HIV-negative MSM on PrEP. In a setting where undiagnosed HIV is high (11), if serosorting is associated with more condomless sex (23), HIV-negative MSM not on PrEP could face an even higher HIV-acquisition risk (11). Thus, with potential changes in sexual mixing because of PrEP, it is even more important to ensure high or increased rates of HIV testing to reduce the fraction or person-years of undiagnosed HIV in the population.

Finally, our findings have important implications for the transmission of sexually transmitted bacteria and other viruses. For example, bacterial sexually transmitted infections, such as syphilis, and viral infections, such as hepatitis C, are disproportionately higher among HIV-positive MSM (36, 37), which could be due in part to population-level serosorting (38). Our observed patterns of sexual mixing related to PrEP could potentially modify the difference in rates of sexually transmitted infections according to HIV status (38).

Our study has several limitations. First, measures of the number and characteristics of sexual partners were subject to recall and reporting bias, especially when respondents were asked to recall information over the period of half a year. However, similar results from event-level and previous-6-month data suggest minimal influence of recall bias on the results. Second, population-level PrEP-matching was restricted to recent partnerships and might not reflect the mixing pattern among all previous-6-month partnerships. This was restricted by lack of data on all partners' PrEP-use status in the previous 6 months. Third, we did not simultaneously consider the influence of viral suppression on sexual mixing; only 33 HIV-positive MSM were not virally suppressed in our study, limiting the analytical power. Fourth, although our results suggest individuals' preferential partner selection according to HIV status and PrEP use, we cannot infer which subset of MSM intended to do so. For example, even if only HIV-positive MSM intended to serosort, and HIV-negative MSM did not, we would still observe serosorting at the population level for both subgroups as a result of partnership-balancing. Therefore, population-level measures of sexual mixing complement but cannot replace individual-level measures of preferential partner selection. Fifth, our approach is limited by the extent to which it subsumes layers of heterogeneity that could be associated with differences in preferential partner selection, including race, age, and socioeconomic status (39). Future studies can apply the same approach to examine sexual mixing according to these attributes. Sixth, we cannot ascertain the temporality in the relationships we observed due to the cross-sectional study design. For example, we cannot distinguish whether being part of a certain sexual network before PrEP uptake influenced the likelihood of PrEP initiation or whether starting PrEP influenced individuals' sexual network. Future studies using longitudinal data could examine potential reasons underlying PrEP-matching. Finally, our results from the RDS-weighted analyses are subject to limitations of the RDS recruitment and statistical adjustment methods (40). For instance, there might be measurement error in respondents' self-reported social network size, which was used to produce weights in RDS-adjusted analysis to account for selection bias (40).

Our findings demonstrate population-level serosorting among both HIV-negative and HIV-positive MSM, in a setting where the majority of HIV-positive MSM are virally suppressed. Our findings also suggest potential influence of PrEP on sexual mixing patterns as evidenced by less population-level serosorting among those on PrEP and PrEP-matching. These data reinforce the importance of monitoring changes in sexual mixing patterns among MSM to inform PrEP implementation and impact evaluation.

University of Toronto, Toronto, Ontario, Canada (Daniel Grace, Ann N. Burchell, Trevor A. Hart); Department of Psychology, Ryerson University, Toronto, Ontario, Canada (Ricky Rodrigues, Syed W. Noor, Trevor A. Hart); Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada (Joseph Cox, Herak Apelian, Marc Messier-Peet); School of Public Health and Social Policy, University of Victoria, Victoria, British Columbia, Canada (Nathan J. Lachowsky); British Columbia Centre for Excellence in HIV/AIDS, Vancouver, British Columbia, Canada (Nathan J. Lachowsky, Heather L. Armstrong, David M. Moore); School of Psychology, University of Southampton, Southampton, United Kingdom (Heather L. Armstrong); Department of Medicine, University of Toronto, Toronto, Ontario, Canada (Darrell H. S. Tan, Sharmistha Mishra); Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Ontario, Canada (Darrell H. S. Tan, Sharmistha Mishra); Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada (Ann N. Burchell); Community-Based Research Centre, Vancouver, British Columbia, Canada (Jody Jollimore); Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland (Stefan Baral); Department of Medicine, Division of AIDS, University of British Columbia, Vancouver, British Columbia, Canada (David M. Moore); and Institute of Medical Sciences, University of Toronto, Toronto, Ontario, Canada (Sharmistha Mishra).

REFERENCES

1. Beyrer C, Baral SD, van Griensven F, et al. Global epidemiology of HIV infection in men who have sex with men. *Lancet*. 2012;380(9839):367–377.

2. Snowden JM, Raymond HF, McFarland W. Seroadaptive behaviours among men who have sex with men in San Francisco: the situation in 2008. *Sex Transm Infect*. 2011;87(2):162–164.

3. Velter A, Bouyssou-Michel A, Arnaud A, et al. Do men who have sex with men use serosorting with casual partners in France? Results of a nationwide survey (ANRS-EN17-Presse Gay 2004). *Euro Surveill*. 2009;14(47):.

4. Cassels S, Katz DA. Seroadaptation among men who have sex with men: emerging research themes. *Curr HIV/AIDS Rep*. 2013;10(4):305–313.

5. Rodriguez-Hart C, Liu H, Nowak RG, et al. Serosorting and sexual risk for HIV infection at the ego-alter dyadic level: an egocentric sexual network study among MSM in Nigeria. *AIDS Behav*. 2016;20(11):2762–2771.

6. Lachowsky NJ, Lin SY, Hull MW, et al. Pre-exposure prophylaxis awareness among gay and other men who have sex with men in Vancouver, BC, Canada. *AIDS Behav*. 2016; 20(7):1408–1422.

7. Grov C, Jonathan Rendina H, Patel VV, et al. Prevalence of and factors associated with the use of HIV serosorting and other biomedical prevention strategies among men who have sex with men in a US Nationwide survey. *AIDS Behav*. 2018;22(8):2743–2755.

8. Martinez JE, Jonas KJ. Pre-exposure prophylaxis sorting among men who have sex with men. *AIDS Care*. 2019;31(3):388–396.

9. Newcomb ME, Mongrella MC, Weis B, et al. Partner disclosure of PrEP use and undetectable viral load on geosocial networking apps: frequency of disclosure and decisions about condomless sex. *J Acquir Immune Defic Syndr*. 2016;71(2):200–206.

10. Grace D, Jollimore J, MacPherson P, et al. The pre-exposure prophylaxis-stigma paradox: learning from Canada's first wave of PrEP users. *AIDS Patient Care STDS*. 2018;32(1):24–30.

11. Wilson DP, Regan DG, Heymer KJ, et al. Serosorting may increase the risk of HIV acquisition among men who have sex with men. *Sex Transm Dis*. 2010;37(1):13–17.

12. Cassels S, Menza TW, Goodreau SM, et al. HIV serosorting as a harm reduction strategy: evidence from Seattle, Washington. *AIDS*. 2009;23(18):2497–2506.

13. Purcell DW, Higa D, Mizuno Y, et al. Quantifying the harms and benefits from serosorting among HIV-negative gay and bisexual men: a systematic review and meta-analysis. *AIDS Behav*. 2017;21(10):2835–2843.

14. Moqueet N SA, Baral S, Tan DHS, et al. Modeling pre-exposure prophylaxis (PrEP) and the influence of sexual mixing patterns on HIV epidemics among men who have sex with men (MSM) [abstract]. *Presented at the 27th Annual Canadian Conference on HIV/AIDS Research*, Vancouver, BC, Canada, April 26–29, 2018.

15. Golden MR, Stekler J, Hughes JP, et al. HIV serosorting in men who have sex with men: is it safe? *J Acquir Immune Defic Syndr*. 2008;49(2):212–218.

16. Snowden JM, Raymond HF, McFarland W. Prevalence of seroadaptive behaviours of men who have sex with men, San Francisco, 2004. *Sex Transm Infect*. 2009;85(6): 469–476.

17. Khosropour CM, Dombrowski JC, Swanson F, et al. Trends in serosorting and the association with HIV/STI risk over time among men who have sex with men. *J Acquir Immune Defic Syndr*. 2016;72(2):189–197.

18. Crepaz N, Marks G, Liau A, et al. Prevalence of unprotected anal intercourse among HIV-diagnosed MSM in the United States: a meta-analysis. *AIDS*. 2009;23(13):1617–1629.

19. McFarland W, Chen YH, Nguyen B, et al. Behavior, intention or chance? A longitudinal study of HIV seroadaptive behaviors, abstinence and condom use. *AIDS Behav*. 2012;16(1):121–131.
20. Khosropour CM, Dombrowski JC, Hughes JP, et al. Operationalizing the measurement of seroadaptive behaviors: a comparison of reported sexual behaviors and purposely-adopted behaviors among men who have sex with men (MSM) in Seattle. *AIDS Behav*. 2017;21(10):2935–2944.
21. Fendrich M, Mackesy-Amiti ME, Johnson TP, et al. Sexual risk behavior and drug use in two Chicago samples of men who have sex with men: 1997 vs. 2002. *J Urban Health*. 2010;87(3):452–466.
22. Grov C, Rendina HJ, Moody RL, et al. HIV serosorting, status disclosure, and strategic positioning among highly sexually active gay and bisexual men. *AIDS Patient Care STDS*. 2015;29(10):559–568.
23. Siegler AJ, Sullivan PS, Khosropour CM, et al. The role of intent in serosorting behaviors among men who have sex with men sexual partnerships. *J Acquir Immune Defic Syndr*. 2013;64(3):307–314.
24. Chen YH, Vallabhaneni S, Raymond HF, et al. Predictors of serosorting and intention to serosort among men who have sex with men, San Francisco. *AIDS Educ Prev*. 2012;24(6):564–573.
25. Garnett GP, Anderson RM. Balancing sexual partnerships in an age and activity stratified model of HIV transmission in heterosexual populations. *IMA J Math Appl Med Biol*. 1994;11(3):161–192.
26. Heckathorn DD. Respondent-driven sampling: a new approach to the study of hidden populations. *Soc Probl*. 1997;44(2):174–199.
27. World Health Organization. *Introduction to HIV/AIDS and Sexually Transmitted Infection Surveillance: Module 4: Introduction to Respondent-Driven Sampling*. Cairo, Egypt: World Health Organization Regional Office for the Eastern Mediterranean; 2013.
28. Lambert G, Cox J, Messier-Peet M, et al. *Engage Montréal: Portrait of the Sexual Health of Men Who Have Sex With Men in Greater Montréal—Cycle 2017–2018, Highlights*. Montreal, QC, Canada: Direction régionale de santé publique, CIUSSS du Centre-Sud-de-l'Île-de-Montréal; 2019.
29. Hanneman R, Riddle M. *Introduction to Social Network Methods*. Riverside, CA: University of California, Riverside; 2005.
30. Volz EHD. Probability based estimation theory for respondent driven sampling. *J Off Stat*. 2008;24(1):79–97.
31. Delva W, Helleringer S. Beyond risk compensation: clusters of antiretroviral treatment (ART) users in sexual networks can modify the impact of ART on HIV incidence. *PLoS One*. 2016;11(9):e0163159.
32. Tan DH SA, Lawless J, Grennan T, et al. High adherence but modest risk compensation among MSM in a PrEP demonstration project [abstract]. Presented at the 25th Annual Canadian Conference on HIV/AIDS Research, Winnipeg, MB, Canada, May 12–15, 2016.
33. Ayala G, Santos GM, Arreola S, et al. Blue-ribbon boys: factors associated with PrEP use, ART use and undetectable viral load among gay app users across six regions of the world. *J Int AIDS Soc*. 2018;21(suppl 5):e25130.
34. Patel RR, Mena L, Nunn A, et al. Impact of insurance coverage on utilization of pre-exposure prophylaxis for HIV prevention. *PLoS One*. 2017;12(5):e0178737.
35. Grace D, Chown SA, Jollimore J, et al. HIV-negative gay men's accounts of using context-dependent sero-adaptive strategies. *Cult Health Sex*. 2014;16(3):316–330.
36. Public Health Agency of Canada. *Syphilis Among Gay, Bisexual, Two-Spirit and Other Men Who Have Sex With Men: a Resource for Population-Specific Prevention*. Ottawa, ON, Canada: Public Health Agency of Canada; 2015.
37. Burchell AN, Gardner SL, Mazzulli T, et al. Hepatitis C virus seroconversion among HIV-positive men who have sex with men with no history of injection drug use: results from a clinical HIV cohort. *Can J Infect Dis Med Microbiol*. 2015;26(1):17–22.
38. MacGregor L, Martin NK, Mukandavire C, et al. Behavioural, not biological, factors drive the HCV epidemic among HIV-positive MSM: HCV and HIV modelling analysis including HCV treatment-as-prevention impact. *Int J Epidemiol*. 2017;46(5):1582–1592.
39. Gesink D, Wang S, Guimond T, et al. Conceptualizing Geosexual archetypes: mapping the sexual travels and egocentric sexual networks of gay and bisexual men in Toronto, Canada. *Sex Transm Dis*. 2018;45(6):368–373.
40. Goel S, Salganik MJ. Assessing respondent-driven sampling. *Proc Natl Acad Sci U S A*. 2010;107(15):6743–6747.