American Journal of Men's Health
May-June 1–8

DOI: 10.1177/15579883211018917
journals.sagepub.com/home/jmh
SAGE

Incidence of Sexually Transmitted Infections After Initiating HIV Pre-Exposure Prophylaxis Among MSM in Southern Denmark

Masoumeh Azarnoosh[1], Isik Somuncu Johansen[1,2], and Raquel Martin-Iguacel[1,2,3]

Abstract

Pre-exposure prophylaxis (PrEP) is a new preventive treatment for individuals at high-risk for HIV infection, such as men who has sex with men (MSM). Studies have confirmed the efficacy but concerns about the potential induction of risk compensation remains. We aimed to assess the incidence of sexually transmitted infections (STIs) after PrEP initiation as a proxy for sexual risk behavior.

This case-crossover study used data from medical records and from the Danish Microbiology Database from patients who initiated PrEP at the Region of Southern Denmark between 2017 and 2019. Poisson regression was used to assess STI incidence 6 months after PrEP initiation versus the 6 months before. To identify potential risk factors, we compared individuals with an increased STI incidence after PrEP initiation with those without, using logistic regression. In total, 46 MSM initiated PrEP in the study period. We found a significant increase in the number of positive samples for STI after PrEP initiation (IRR 1.83; 95% CI [1.03, 3.26]) and a tendency for higher incidence of STI episodes (1.67; 95% CI [0.91, 3.13]). The increase was concentrated to a group of users, but no significant correlation was found between increasing incidence and the baseline factors examined.

We observed a degree of risk compensation after the implementation of PrEP among MSM, clustering to a group of users. Our results highlight the importance of frequent STI screening among MSM on PrEP as timely diagnosis could contribute to an overall decrease in STI incidence and incidence among MSM.

Keywords

PrEP, STI, sexually transmitted infections, MSM, gonorrhea, chlamydia, syphilis

Received March 12, 2021; revised April 24, 2021; accepted April 27, 2021

In 2012, the combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) was approved by the US Food and Drug Administration (FDA) for use as primary prevention to reduce the risk of HIV acquisition in high-risk populations, so-called pre-exposure prophylaxis (PrEP). In 2016, the European Medicines Agency (EMA) recommended approval of PrEP in EU, and it has been officially recommended by the Danish Health Authorities since September 2018, as a supplement to the existing prevention efforts.

PrEP is a daily or on-demand regimen of antiretroviral agents that has demonstrated to effectively reduce the transmission of HIV among at-risk populations when high medication adherence in maintained (Fonner et al., 2016; McCormack et al., 2016; Molina et al., 2017). While the preventive effect of PrEP in reducing HIV acquisition is a success, it has raised concerns about patients' possible sexual behavioral changes, as well as

[1]Infectious Diseases Department, Odense University Hospital, Odense C, Denmark
[2]Research Unit for Infectious Diseases, Odense University Hospital, University of Southern Denmark, Denmark
[3]OPEN, The Open Patient Data Explorative Network, the Department of Clinical Research, University of Southern, Denmark

Corresponding Author:
Raquel Martín Iguacel, Infectious Diseases Department, Odense University Hospital, J. B. Winsløws Vej 4, Odense C, 5000, Denmark.
Email: raquel@bisaurin.org

the potential short- and long-term side effects (Catherine et al., 2017; Holt & Murphy, 2017; Marcus et al., 2013, 2016; Montaño et al., 2019). PrEP users' behavioral changes may result in more risky sexual practices and decline in condom use, which could increase the risk of other sexually transmitted diseases (STIs), a phenomenon known as risk compensation. Various studies have investigated risk compensation after PrEP initiation, with mixed results (Catherine et al., 2017; Grant et al., 2014; Marcus et al., 2016b; Molina et al., 2017; Montaño et al., 2019; Ramchandani & Golden, 2019; Traeger et al., 2018). In several randomized placebo controlled double-blinded trials, self-reported condom use and number of STI remained unchanged during the trial period (Fonner et al., 2016; McCormack et al., 2016). In open-label studies, where users knew they were receiving PrEP, an increase in condomless sex and STI has been reported, especially in later studies, possibly due to increased acceptance of PrEP and its efficacy preventing HIV infection over time (Traeger et al., 2018, 2019). Also, at the community level, one observational study reported a decrease in condom use paralleling the increase in PrEP coverage among MSM, reflecting a decrease in risk perception (Holt et al., 2018).

The purpose of the present study was to describe the incidence of STI in the period before and after PrEP initiation in the first patients treated in the region of Southern Denmark.

Methods

The Department of Infectious Diseases at Odense University Hospital covers the region of Southern Denmark with a population of 1.2 million people in 2019 and offers PrEP to people at high risk of HIV infection, based on an individual assessment. Before PrEP initiation, subjects are evaluated to rule out medical contraindications, including HIV infection. All eligible subjects are examined at PrEP initiation and then every 3 months for clinical and biochemical control, and screening for STI, which includes gonorrhea, chlamydia, syphilis.

Study Period

The study ran from April 2017 through August 2019. The individual participants were followed from 6 months prior to PrEP initiation until 6 months after.

Study Design

The study had a case crossover design with an intention-to-treat analysis to assess changes in STI incidence between the periods before and after PrEP initiation. Participants served as their own control.

Study Population

We included all person ≥18 years old who were at high risk of acquiring HIV infection and who initiated PrEP in the Region of Southern Denmark. All participants initiated daily PrEP.

Outcome

We assessed the incidence of chlamydia, gonorrhea, and syphilis during the 6 months before PrEP initiation (pre-PrEP) compared to 6 months after (post-PrEP). Information on STI was gathered from patient records and the Danish microbiology database (MIBA).

Statistical Analyses

For all participants, we included the following baseline variables: age at PrEP initiation, gender, sexual orientation, steady partner, number of self-reported condomless anal sex contacts 12 weeks prior to PrEP initiation, drug and alcohol consumption, use of post-exposure prophylaxis (PEP) or PrEP before study inclusion, pre-study STI, history of viral hepatitis, hepatitis vaccination, and comorbidity.

We collected information on medication adherence, PrEP side effects, use of other drugs during the study period, and significant interactions between them.

For gonorrhea and chlamydia, we recorded data for all positive specimens/body localizations (urethral, rectal, pharyngeal) and STI episodes. Samples from different body locations but collected on the same date were considered one episode and one treatment and defined as an STI episode. For syphilis, we recorded incidence during the period, and at what stage it was diagnosed. For HIV, we recorded incidence at the end of the study.

Mixed-effects Poisson regression models were used to calculate the STI incidence in the period before and after PrEP initiation. Predictors in the model included the period variable (pre- or post-PrEP) and STI tests (e.g., rectal, urethral, or pharyngeal gonorrhea/chlamydia or syphilis) or STI episodes (gonorrhea, chlamydia, or syphilis) and the interaction between these two variables. We calculated the incidence rate ratio (IRR) with 95% CI.

We used logistic regression to compare individuals with an increased incidence of STI in post-PrEP versus pre-PrEP, with individuals without an increase in incidence of STI between these periods, to identify possible risk factors that could predict an increased risk. We calculated odds ratio (OR) with 95% CI.

Data analysis was performed using software Stata v.16.

Ethics. All participants provided a written informed consent. The Danish Data Protection Agency has granted

permission (19/42621). Ethics approval is not required by Danish legislation governing for this type of research.

Results

A total of 46 individuals started PrEP in the study period and were included in the study. Baseline characteristics are presented in Table 1. Most participants (n = 45, 97.8%) were MSM. The median age at PrEP initiation was 39 years (interquartile range, IQR, 35–48). Most participants were 30–49 years old (69.4%), but there were nine participants (19.8%) aged ≥50 years. Half of the participants (n = 23, 50.0%) did not have a steady partner and 52.2% (n = 24) had 1–10 self-reported episodes of condomless anal sex in the 12 weeks before PrEP initiation. Six participants (16%) reported non-injection drug use, and one person (2.2%) had been in PEP before the study. Nineteen participants (41.3%) had neither STI before nor after PrEP initiation during the study period. Fourteen (30.4%) participants had been diagnosed with at least one STI during the 6 months prior to initiation of PrEP, 13 of whom were diagnosed with one and one participant with multiple STI. In the post-PrEP period, 20 participants (43.5%) were diagnosed with at least one STI (42% increase), 14 with a single case, and six with more (Table 2).

Five participants (10.9%) were already on PrEP before study inclusion, and five (10.9%) were only followed for 5 months after PrEP initiation. We found similar results when we exclude them from the analysis (data not reported).

Twelve participants (26.1%) had concomitant comorbidities receiving another medication: one with ADHD, three with depression, three with diabetes, three with hypertension, one with reflux, and one with hypercholesterolemia (Table 1).

Only mild gastrointestinal side effects were reported during the study period, nausea being the most common. One participant reported non-adherence related to adverse drug reactions, while the remaining 45 participants (97.8%) all reported complete adherence. Among the 10 individuals taking other medications (21.7%), no interactions were found.

We observed an increased incidence of positive samples for STI of 143.5 per 100 person-years, in the post-PrEP period, compared with 78 per 100 person-years in pre-PrEP period (IRR = 1.83; 95% CI [1.03, 3.26]) and STI episodes with an incidence of 117.4 per 100 person-years in the post-PrEP period compared with 69.5 per 100 person-years in the pre-PrEP period (IRR = 1.69; 95% CI [0.91, 3.13]; Table 3).

Table 4 illustrates the study population divided into two subgroups. One group consisted of participants with increased incidence of STI in the post-PrEP period compared to the pre-PrEP period, while the other group included participants with no change in incidence between

Table 1. Demographics of Men Who Have Sex With Men (MSM) Initiating Pre-Exposure Prophylaxis (PrEP) in the Region of Southern Denmark (n = 46).

	Participants, *N*	%
Median age at PrEP initiation (IQR)	39 (35–48)	
Age (years)		
<25	4	8.7
25–29	1	2.2
30–39	19	41.3
40–49	13	28.3
>= 50	9	19.6
Gender		
Men	46	100
Current steady sex partner		
Steady partner	12	26.1
No steady partner	23	50.0
Not informed	11	23.9
Sexual orientation		
MSM	45	97.8
Bisexual men	1	2.2
Self-reported number of condomless anal sex		
0	1	2.2
1–10	24	52.2
11–20	6	13.0
>20	3	6.5
Not informed	12	26.1
Drug use		
Intravenous drug use	0	0 (0)
Recreational drugs	6	13.0
Alcohol (units pr. week)		
< 7/14	16	34.8
> 7/14	2	4.3
Not informed	28	60.9
Post-exposure prophylaxis (PEP) before study inclusion	1	2.2
PrEP before study inclusion	5	10.9
Documented STI diagnosis before study inclusion		
Yes	20	43.5
No	26	56.5
Previous acute viral hepatitis		
A	1	2.2
B	1	2.2
Not informed	9	19.6
Hepatitis vaccination before study inclusion		
A	15	32.6
B	10	21.7
Comorbidities		
None	34	73.9
Attention deficit hyperactivity disorder (ADHD)	1	2.2
Depression	3	6.5
Diabetes mellitus	3	6.5
Arterial hypertension	3	6.5
Gastroesophageal reflux	1	2.2
Hypercholesterolemia	1	2.2

Note: N, number of participants; IQR, interquartile range; STI, sexually transmitted infections.

Table 2. Number of Participants With Sexually Transmitted Infections in the Pre-PrEP and Post-PrEP Period.

	N (%)	1 positive sample for STI (*n*)	>1 positive sample for STI (*n*)	1 treatment for STI (*n*)	>1 treatment for STI (*n*)
Participants without STI in the pre-PrEP or post-PrEP period	19 (41.3)	-	-	-	-
Pre-PrEP period: participants with at least one STI	14 (30.4)	11	3	13	1
Post-PrEP period: participants with at least one STI	20 (43.4)	11	9	14	6

Note: STI, sexually transmitted infections; pre-PrEP, 6 months period before pre-exposure prophylaxis initiation; post-PrEP, 6 months period after pre-exposure prophylaxis initiation.

Table 3. Incidence of Sexually Transmitted Infections Among Men Who Have Sex With Men (MSM) Initiating PrEP in the Region of Southern Denmark ($n = 46$).

	Pre-PrEP Period		Post-PrEP Period			
	N	Pre-PrEP incidence (STI per 100 person-years)	N	Post-PrEP incidence (STI per 100 person-years)	IRR (95% CI)	*p* value
Total positive STI samples	18	78.0	33	143.5	1.83 (1.03–3.26)	.039
Total STI treatments	16	69.5	27	117.4	1.69 (0.91–3.13)	.097
Syphilis	1	4.3	5	21.7	5.00 (0.58–42.80)	.14
Primary	0	-	3	13.0		
Secondary	0	-	0	-		
Latent	1	4.3	2	8.7		
Gonorrhea, number of treatments	7	30.4	10	43.5	1.43 (0.54–3.75)	.76
Gonorrhea, number of samples	9	39.1	14	60.8	1.56 (0.67–3.59)	.301
Urethral	2	8.7	3	13.0		
Rectal	3	13.0	4	17.4		
Pharyngeal	4	17.4	7	30.4		
Chlamydia, number of treatments	8	34.8	12	52.2	1.50 (0.61–3.67)	.374
Chlamydia, number of samples	8	34.8	14	60.8	1.75 (0.73–4.17)	.207
Urethral	2	8.7	1	4.3		
Rectal	6	26.1	11	47.8		
Pharyngeal	0	-	2	8.7		

Note: STI, sexually transmitted infections; PrEP, pre-exposure prophylaxis; pre-PrEP, 6 months period before pre-exposure prophylaxis initiation; post-PrEP, 6 months period after pre-exposure prophylaxis initiation; IRR, incidence rate ratio; CI, confidence interval; N, number of participants.

the periods. These groups were compared to identify risk factors for increased incidence of STI. No statistically significant differences were found between the groups with the regard the baseline variables examined.

Table 4. Comparison of Baseline Characteristics Between Participants With an Increase in Sexually Transmitted Infections' Incidence After PrEP Initiation and Those Without.

	Participants With Increased Incidence of STI in Post-PrEP Compared With Pre-PrEP Period $n = 15$ (32.6%)	Participants Without Increased Incidence of STI in Post-PrEP Compared With Pre-PrEP Period $n = 31$ (67,4%)	OR (95% CI)	p value
Median age at PrEP initiation (IQR)	43 (31–51)	39 (35–44)	1.00 (0.96–1.04)	.969
Intravenous drug use	0	0	-	-
Recreational drug use	3 (50%)	3 (50%)	2.33 (0.41–13.3)	.339
PrEP before study inclusion	3 (60%)	2 (40%)	3.62 (0.54–24.5)	.187
PEP before study inclusion	0 (0%)	1 (100%)	-	-
Current steady partner	5 (41.7%)	7 (58.3%)	1.71 (0.44–6.71)	.439
Alcohol overconsumption	2 (100%)	0	-	-
STI before study inclusion	6 (30%)	14 (70%)	0.81 (0.23–2.83)	.741
Condomless sexual contact >10 in the last 12 weeks	7 (33.3%)	14 (66.7%)	1.21 (0.34–4.30)	.763

Note. STI, sexually transmitted infections; PrEP, pre-exposure prophylaxis; pre-PrEP, 6 months period before pre-exposure prophylaxis initiation; post-PrEP, 6 months period after pre-exposure prophylaxis initiation; OR, odds ratio; CI, confidence interval; *N*, number of participants; IQR, interquartile range.

Discussion

In our study, we identified PrEP use to be associated with an increase in the number of patients diagnosed with STI and STI diagnoses. STIs were concentrated in a subgroup of PrEP users, with a risk of re-infection. There was a trend toward an increasing incidence of gonorrhea, chlamydia, and syphilis after PrEP start, when examined individually, however, without achieving statistical significance. Overall, these findings suggest that PrEP start was associated with a change in risk behavior in a subgroup of patients.

Previous studies have identified that rectal STI may be a marker of condomless anal sex with a consequent greater risk of HIV infection (Varghese et al., 2001; Vitinghoff et al., 1999). In our study, we observed an 83% increase in the incidence of positive rectal samples for chlamydia in the post-PrEP period, which could indicate increasing activity of condomless receptive anal sex after initiation of PrEP. We also observed a 56% increase in the incidence of gonorrhea positive samples. With regard to syphilis, we observed a five-fold increased incidence, but the absolute numbers are small. All cases were diagnosed at an early stage. The transmission of syphilis can occur despite condom use, as the syphilis chancres are formed not only on the genitals but also on other areas of the body (rectum, lips, mouth) that are not necessarily protected by the use of a condom.

Results from randomized placebo-controlled double-blind studies, failing to detect an increase in condomless sex or STI, should be interpreted with caution, as risk compensation relies on the idea that knowledge of being on preventive treatment reduces the individual perception of risk. An increase in condomless sex and STI has been described in several open-label studies, where users knew that they were on PrEP. A recent meta-analysis reported that PrEP use was associated with an increased incidence of STI (OR 1.24; 95% CI [0.99, 1.54]) and especially rectal chlamydia (OR 1.59; 95% CI [1.19, 2.13]). This association was stronger in more recent studies and in studies with longer follow-up, which could reflect an increasing confidence among PrEP users in PrEP efficacy and a more widespread use of PrEP among at-risk populations and with that, a lower perception of risk (Traeger et al., 2018). A cohort study of 211 MSM in Los Angeles also identified an increase in the incidence of rectal chlamydia (RR 1.83; 95% CI [1.13, 2.98]) and syphilis (RR 2.97; 95% CI [1.23, 7.18]) after PrEP initiation (Beymer et al., 2018). Our findings are in line with these studies, suggesting a degree of risk compensation among subjects after initiating PrEP in a real-world setting. Furthermore, there is some degree of evidence of community-level risk compensation as PrEP use is more widespread among MSM (Holt et al., 2018)

Risk compensation might be clustering in subgroup of users with certain risk factors. In this study, we were

unable to identify specific risk factors for increasing STI incidence compared to persons with no increase in STI following PrEP start, based on the baseline variables collected. Other studies have reported that younger age, chem sex, multiple partners, and group sex are associated with more frequent unprotected anal sex and thus a higher risk for STIs (Drückler et al., 2018; Hoornenborg et al., 2018). However, more frequent screening among PrEP users could in itself also contribute to the observed increased incidence (Chow et al., 2017; Cornelisse et al., 2017; Ramchandani & Golden, 2019).

In general, PrEP was well tolerated, and only 9% of study participants experienced mild and self-limiting gastrointestinal side effects, primarily during the first month after initiation. We found no evidence of increased serum creatinine during the study period, but the follow-up time was very short.

No participant was infected with HIV during the study period. The studies IPrEx and Ipergay have reported that HIV effectiveness is directly linked to a constant level of medication in the blood (Grant et al., 2014; Molina et al., 2017). Taking 4–7 tablets of TDF-FTC per week was associated with a 100% reduction in HIV incidence among MSM PrEP users (95% CI [86, 100%]) (Grant et al., 2014).

Our study has a few limitations. The sample size was small with the risk of type II error and thus less strength to detect any difference in incidence between periods. In particular, the number of patients in the sub-analyses (STI subgroups) became very small, and the study did not have the strength to draw reliable conclusions in these subgroups.

We looked at two periods of 6 months. A longer observation period could potentially have increased the validity of the study in terms of a more accurate measurement of the number of STIs as a proxy for risk behavior. In the post-PrEP period, we measured incident cases and participants were routinely screened every 3 months. In the pre-PrEP period, prevalent cases were recorded, and participants were screened in case of symptoms or risk of infection as well as at the onset of PrEP, and screening frequency in the two periods were thus not the same. Confounding due to different STI testing frequency during the two periods cannot be excluded. Furthermore, we have interpreted STIs as a surrogate marker for behavioral changes and risk compensation among MSM initiating PrEP. We cannot rule out that the increase observed in STIs was as least partially due to a wider community-level risk compensation among MSM, as PrEP availability becomes more widespread, and as such not related to behavioral changes for the individual.

With the low number of participants, our case-crossover design is a strength, given that participants acted as their own control. Besides, we included all the individuals starting PrEP in our Region during the study period.

This study is a small real-world case-crossover study, where 46 MSM were followed during the first 6 months after PrEP initiation in the Region of Southern Denmark. We observed a clustering of STIs in a subgroup of patients as well as a statistically significant 83% increase in the total number of positive STI samples after PrEP initiation, suggesting a degree of risk compensation. When looking at the number of STI treatments, we also found a numerical increase of 69%, however, without achieving statistical significance. These results support the importance of frequent STI screening among MSM on PrEP, as timely diagnosis could contribute to an overall decrease in STI incidence and incidence among MSM. We did not identify specific risk factors for increased incidence of STI, but the number of participants was low. Further studies will be needed to better describe PrEP in clinical practice, confirm the association with STI, as well as elucidate risk factors in order to identify individuals with higher STI risk to provide better preventive efforts.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This trial received no grants. The Danish Data Protection Agency has granted permission (19/42621).

Transparency statement

We hereby declare that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned have been explained.

ORCID iD

Raquel Martin-Iguacel https://orcid.org/0000-0003-3543-1970

References

Beymer, M. R., DeVost, M. A., Weiss, R. E., Dierst-Davies, R., Shover, C. L., Landovitz, R. J., Beniasians, C., Talan, A. J., Flynn, R. P., Krysiak, R., McLaughlin, K., & Bolan, R. K. (2018). Does HIV pre-exposure prophylaxis use lead to a higher incidence of sexually transmitted infections? A case-crossover study of men who have sex with men in Los Angeles, California. *Sexually Transmitted Infections*, *94*(6), 457–462. http://sti.bmj.com/lookup/doi/10.1136/sextrans-2017-053377

Catherine, E., Oldenburg, A. S., Nunn, M. M., Almonte, A., Mena, L., Patel, R. R., Mayer, K. H., & Chan, P. A. (2017). Behavioral changes following uptake of HIV pre-exposure prophylaxis among men who have sex with men in a clinical setting. *Physiology & Behavior*, *176*(1), 139–148. https://doi.org/10.1016/j.physbeh.2017.03.040

Chow, E. P. F., Callander, D., Fairley, C. K., Zhang, L., Donovan, B., Guy, R., Lewis, D. A., Hellard, M., Read, P., Ward, A., Chen, M. Y., & for the ACCESS collaboration (2017). Increased syphilis testing of men who have sex with men: Greater detection of asymptomatic early syphilis and relative reduction in secondary syphilis. *Clinical Infectious Diseases*, *65*(3), 389–395. https://doi.org/10.1093/cid/cix326

Cornelisse, V. J., Chow, E. P. F., Huffam, S., Fairley, C. K., Bissessor, M., De Petra, V., Howden, B. P., Denham, I., Bradshaw, C. S., Williamson, D., & Chen, M. Y. (2017). Increased detection of pharyngeal and rectal gonorrhea in men who have sex with men after transition from culture to nucleic acid amplification testing. *Sexually Transmitted Diseases*, *44*(2), 114–117. https://doi.org/10.1097/OLQ.0000000000000553

Drückler, S., Van Rooijen, M. S., & De Vries, H. J. C. (2018). Chemsex among men who have sex with men: A sexualized drug use survey among clients of the sexually transmitted infection outpatient clinic and users of a gay dating app in Amsterdam, the Netherlands. *Sexually Transmitted Diseases*, *45*(5), 325–331. https://doi.org/10.1097/OLQ.0000000000000753

Fonner, V. A., Dalglish, S. L., Kennedy, C. E., Baggaley, R., O'Reilly, K. R., Koechlin, F. M., Rodolph, M., Hodges-Mameletzis, I., & Grant, R. M. (2016). Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *Aids*, *30*(12), 1973–1983. https://doi.org/10.1097/QAD.0000000000001145

Grant, R. M., Anderson, P. L., McMahan, V., Liu, A., Rivet Amico, K., Mehrotra, M., Hosek, S., Mosquera, C., Casapia, M., Montoya, O., Buchbinder, S., Veloso, V. G., Mayer, K., Chariyalertsak, S., Bekker, L.-G., Kallas, E. G., Schechter, M., Guanira, J., Bushman, L., . . . for the iPreEx study team (2014). An observational study of pre-exposure prophylaxis uptake, sexual practices, and HIV incidence among men and transgender women who have sex with men. *Lancet Infectious Disease*, *14*(9), 15. https://doi.org/10.1016/S1473-3099(14)70847-3

Holt, M., Lea, T., Mao, L., Kolstee, J., Zablotska, I., Duck, T., Allan, B., West, M., Lee, E., Hull, P., Grulich, A., De Wit, J., & Prestage, G. (2018). Community-level changes in condom use and uptake of HIV pre-exposure prophylaxis by gay and bisexual men in Melbourne and Sydney, Australia: results of repeated behavioural surveillance in 2013–17. *The Lancet HIV*, *5*(8), e448–e456. https://doi.org/10.1016/S2352-3018(18)30072-9

Holt, M., & Murphy, D. A. (2017). Individual versus community-level risk compensation following preexposure prophylaxis of HIV. *American Journal of Public Health*, *107*(10), 1568–1571. https://doi.org/10.2105/AJPH.2017.303930

Hoornenborg, E., Coyer, L., Van Laarhoven, A., Achterbergh, R., De Vries, H., Prins, M., & Van Der Loeff, M. S. (2018). Change in sexual risk behaviour after 6 months of pre-exposure prophylaxis use: Results from the Amsterdam pre-exposure prophylaxis demonstration project. *Aids*, *32*(11), 1527–1532. https://doi.org/10.1097/QAD.0000000000001874

Marcus, J. L., Glidden, D. V., Mayer, K. H., Liu, A. Y., Buchbinder, S. P., Amico, K. R., McMahan, V., Kallas, E. G., Montoya-Herrera, O., Pilotto, J., & Grant, R. M. (2013). No Evidence of sexual risk compensation in the iPrEx trial of daily oral HIV preexposure prophylaxis. *PLoS ONE*, *8*(12). https://doi.org/10.1371/journal.pone.0081997

Marcus, J. L., Hurley, L. B., Hare, C. B., Nguyen, D. P., Phengrasamy, T., Silverberg, M. J., Stoltey, J. E., & Volk, J. E. (2016). Preexposure prophylaxis for HIV prevention in a large integrated health care system: Adherence, renal safety, and discontinuation. *Journal of Acquired Immune Deficiency Syndromes (1999)*, 73(5), 540–546. http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=27851714&retmode=ref&cmd=prlinks

McCormack, S., Dunn, D. T., Desai, M., Dolling, D. I., Gafos, M., Gilson, R., Sullivan, A. K., Clarke, A., Reeves, I., Schembri, G., Mackie, N., Bowman, C., Lacey, P. C. J., Apea, V., Brady, M., Fox, J., Taylor, S., Antonucci, S., Khoo, S. H., . . . Gill, O. N. (2016). Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): Effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet*, *387*(10013), 53–60. http://dx.doi.org/10.1016/S0140-6736(15)00056-2

Molina, J. M., Charreau, I., Spire, B., Cotte, L., Chas, J., Capitant, C., Tremblay, C., Rojas-Castro, D., Cua, E., Pasquet, A., Bernaud, C., Pintado, C., Delaugerre, C., Sagaon-Teyssier, L., Le Mestre, S., Chidiac, C., Pialoux, G., Ponscarme, D., Fonsart, J., . . . for the ANRS IPERGAY Study Group (2017). Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *The Lancet HIV*, *4*(9), e402–e410. https://doi.org/10.1016/S2352-3018(17)30089-9

Montaño, M. A., Dombrowski, J. C., Dasgupta, S., Golden, M. R., Duerr, A., Manhart, L. E., Barbee, L. A., & Khosropour, C. M. (2019). Changes in sexual behavior and STI diagnoses among MSM initiating PrEP in a clinic setting. *AIDS and Behavior*, *23*(2), 548–555. https://doi.org/10.1007/s10461-018-2252-9

Ramchandani, M. S., & Golden, M. R. (2019). *Confronting rising STIs in the Era of PrEP and treatment as prevention*. 1–13. papers3://publication/doi/10.1007/s11904-019-00446-5

Traeger, M. W., Cornelisse, V. J., Asselin, J., Price, B., Roth, N. J., Willcox, J., Tee, B. K., Fairley, C. K., Chang, C. C., Armishaw, J., Vujovic, O., Penn, M., Cundill, P., Forgan-Smith, G., Gall, J., Pickett, C., Lal, L., Mak, A., Spelman, T. D., . . . for the PrEPX Study Team (2019). Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. *JAMA: The Journal of the American*

Medical Association, *321*(14), 1380. http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2019.2947

Traeger, M. W., Schroeder, S. E., Wright, E. J., Hellard, M. E., Cornelisse, V. J., Doyle, J. S., & Stoové, M. A. (2018). 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. *Clinical Infectious Diseases*, *67*(5), 676–686. https://doi.org/10.1093/cid/ciy182

Varghese, B., Maher, J. E., Peterman, T. A., Branson, B. M., & Steketee, R. W. (2001). *Reducing the Risk of Sexual HIV Transmission the Per-Act Risk for HIV on the Basis of Choice of Partner*, 38–43.

Vitinghoff, E., Douglas, J., Judon, F., McKiman, D., MacQueen, K., & Buchinder, S. P. (1999). Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *American Journal of Epidemiology*, *150*(3), 306–311. https://doi.org/10.1093/oxfordjournals.aje.a010003