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Who should be offered HIV pre-exposure prophylaxis (PrEP)?: A secondary analysis of a Phase 3 PrEP efficacy trial in men who have sex with men and transgender women

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Abstract

Background—Pre-exposure prophylaxis (PrEP) has been proven to reduce HIV acquisition in men who have sex with men and transgender women (MSM/TGW). For maximal impact, PrEP should be targeted to subpopulations accounting for the largest proportion of infections (population attributable fraction, PAF) and for whom the number needed to treat (NNT) to prevent infection is lowest.

Methods—The iPrEx study was a randomized controlled efficacy trial of tenofovir-disoproxil-fumarate/emtricitabine PrEP in 2499 MSM/TGW on 4 continents. We calculated the association between demographic and risk behavior during screening with subsequent seroconversion among placebo recipients using a Poisson model, and the PAF and NNT for risk behavior subgroups.

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Findings—Of 1248 placebo participants enrolled, 83 became HIV infected in follow-up. Participants reporting non-condom receptive anal intercourse (ncRAI) seroconverted significantly more often than MSM/TGW reporting no condomless anal sex (adjusted hazard ratio (AHR) 5·11, 95% CI 1·55-16·79). The overall PAF for MSM/TGW reporting ncRAI was 64% (prevalence=60%). Most of this risk came from ncRAI with unknown serostatus partners (PAF 53%, prevalence=54%, AHR 4·76); in contrast, the PAF for ncRAI with an HIV positive partner, an uncommon practice, was only 1% (prevalence 1%, AHR=7·11). The overall NNT per year for the cohort was 62 (95% CI 44-147). NNTs were lower for MSM/TGW self-reporting ncRAI, cocaine use, or a sexually transmitted infection (NNT= 36, 12, and 41 respectively). Having a single partner or non-condom insertive anal sex had the highest NNTs.

Interpretation—PrEP may be most effective at a population level if targeted toward MSM/TGW reporting ncRAI, even with partners perceived to be HIV negative. Substance use history and testing for STIs may also inform individual decisions to start PrEP. Considering PAF and NNT can aid in discussing the benefits and risks of PrEP with MSM/TGW.

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Introduction

Men who have sex with men and transgender women (MSM/TGW) make up the largest proportion of new HIV infections throughout North and South America,[1,2] Western Europe,[3]Asia,[2] and Australia.[4] Despite increases in the frequency of HIV testing, knowledge of HIV serostatus, and access to antiretroviral therapy, infection rates among MSM/TGW are stable or continuing to rise. [2,5] To date, the only biomedical intervention proven to protect against HIV acquisition for MSM/TGW in a randomized controlled trial is pre-exposure prophylaxis (PrEP) ;[6] post-exposure prophylaxis for HIV uninfected and treatment for HIV positive MSM/TGW likely also decrease risk, although neither has been formally evaluated in this population. Condom use can also be considered a biomedical intervention, although data on their effectiveness is limited to analyses of observational data.[7] The iPrEx trial, a randomized, placebo-controlled efficacy trial of daily co-formulated tenofovir disoproxil fumarate/emtricitabine (TDF-FTC) in HIV uninfected MSM/TGW demonstrated a 42% reduction in new infections in men assigned to the active treatment arm, when follow-up of the blinded phase was complete.[6,8] Comparing drug level with studies of directly observed dosing showed that none of the seroconverters had drug levels consistent with daily dosing at the time their infection was detected.[9] In July 2012, the US Food and Drug Administration approved daily TDF-FTC for use as PrEP against sexually acquired HIV infection in high-risk uninfected adults.

The initial Centers for Disease Control and Prevention (CDC) PrEP guidance document recommended offering PrEP to “MSM at substantial, ongoing, high risk for acquiring HIV”[10] and the World Health Organization (WHO) for MSM/TGW “where HIV transmission occurs…and additional HIV prevention choices for them are needed.”[11] However, many providers have difficulty in assessing risk,[12] and neither CDC nor WHO has yet provided specific behavioral criteria for PrEP. Some surveys have found that providers prioritize PrEP for known serodiscordant couples.[13,14] Cost effectiveness modeling suggests that the cost per infection averted is lowest if PrEP is used by the highest risk populations[15] with an annual HIV incidence greater than 2/100 person-years (py).[16] However, each set of models uses different behavioral eligibility criteria for MSM/TGW receiving PrEP, and effectiveness is assumed to be uniform across risk groups.[15,17-19]

Two epidemiologic constructs, the population attributable fraction (PAF) and the number needed to treat (NNT) are complementary strategies for identifying populations who may derive the most benefit from PrEP. PAF combines the relative risk of a characteristic with its prevalence in a given population to determine the proportion of infections associated with (or attributable to) that factor. Although the PAF has been estimated for populations of MSM in Australia,[20] estimates in the US come from studies conducted 10 or more years ago,[21,22] and none exist for TGW nor MSM/TGW in other parts of the world. Determining which subgroups of MSM/TGW have high PAF could help identify those subgroups most important for PrEP to reduce HIV infections at a population level.

The NNT estimates the number of persons who need to receive a treatment in one year to prevent one negative outcome from occurring. In the case of PrEP for MSM/TGW, the NNT refers to the number of men who would need to be given daily TDF-FTC for one year to prevent one HIV infection. This measure is based on both the underlying HIV incidence and PrEP effectiveness within a given population. The NNT has not yet been calculated for subsets of MSM/TGW, and all of the cost effectiveness estimates for MSM/TGW published to date assume a uniform effectiveness across subgroups. Factors associated with a low NNT may be helpful in informing individual doctor-patient decisions regarding taking PrEP.

To identify subpopulations for whom PrEP may have the largest impact, we estimated the PAF and NNT iPrEx study participants, a trial of 2499 MSM/TG from North and South America, Africa and Asia.

Methods

This is secondary analysis of iPrEx study data, a Phase 3 randomized controlled trial of TDF-FTC PrEP, described in detail elsewhere.[6] Briefly, we enrolled 2499 MSM/TGW from 11 trial sites in Peru, Brazil, Ecuador, Thailand, South Africa and the United States. Individuals who were HIV-seronegative, age 18 years or older, male sex at birth (irrespective of current gender identity), without medical contraindications for trial participation, met behavioral risk criteria in the 6 months prior to screening, and were able to provide written informed consent were eligible for participation. Behavioral risk factors included anal sex with at least four (or six, depending on the study site) male partners, a diagnosis of a sexually transmitted infection (STI), engaging in transactional sex, or condomless anal sex with an HIV-positive or unknown-serostatus partner. Participants were randomly assigned to receive a pill with co-formulated TDF-FTC or placebo, to be taken on a daily basis. We followed participants on a monthly basis with HIV antibody testing and medical evaluations. All participants were provided with free condoms and lubricant, given regular risk reduction counseling, and provided linkage to appropriate community and medical services.

Behavioral risk assessment

We collected baseline behavioral risk data at screening by interviewer-administered or computer self-administered (CASI) data collection, using questions adapted from earlier studies in these populations. Interviewers asked questions about total number of male sex partners with whom the participant had oral or anal sex in the previous threemonths, as well as questions about the number of male partners with whom they had engaged in specific sexual practices, stratified by perceived HIV serostatus. Questions about exchange of sex for money, drugs, or services and self-reported sexually transmitted infections covered the previous six months. Through CASI, participants answered questions about drug and alcohol use in the previous month.

Laboratory testing

Study staff performed monthly HIV antibody testing using point-of-care rapid blood tests. All sites used two rapid HIV antibody tests; all reactive tests were confirmed with Western blot or RNA tests.

Statistical analysis

Models for seroconversion were based on the HIV infections through the study treatment period ending 21 November 2010. Because our goal was to identify subgroups of MSM/TGW who might benefit most from PrEP in the future, analyses used baseline rather than time-dependent measures of sexual risk and drug use. Subgroup effectiveness and hazard ratios were estimated from a Poisson model with a log link and offset for follow-up time. Variables with a p-value of <0·20 in univariate analyses were included in the multivariate model.

The PAF for a variable was estimated as:

$$\mathrm{P_e}^{*}(RR1)/(1{+}\mathrm{P_e}^{*}(RR1))$$

where P_e is the prevalence of the exposure and RR is the rate ratio for the factor analyses estimated from a Poisson model for HIV infections estimated from the placebo arm. For a variable with greater than 2 categories, the PAF for the jth category was estimated[23] as

$$p_j\,(RR_j-1)/\sum_{k=1}^{K} p_k RR_k.$$

The number needed to treat was estimated[24] as:

$$\left[exp(-\lambda_{0k}\,(1-E_k/100))-exp(-\lambda_{0k})\right]^{-1}$$

where E_k is the % modified intention-to-treat (mITT) efficacy due to study treatment and lamba0_k is the annual rate of HIV infections on the placebo in the k^{th} stratum.

Role of the funding sources

The National Institute of Allergy and Infectious Diseases and the Bill and Melinda Gates Foundation sponsored this trial; study drug was donated by Gilead Sciences. The corresponding author had full access to all the data and responsibility for the decision to submit for publication. The sponsors approved the study design, but were not involved in the data collection, data analysis, data interpretation, writing of this manuscript, nor the decision to submit for publication.

Results

Of the 2499 MSM/TGW in this study, 1251 were randomized to receive TDF-FTC and 1248 to placebo. Table 1 compares HIV incidence by baseline demographic and behavioral risk characteristics among the placebo group. This cohort was young (median age less than 25 years) and largely recruited from the Andean countries, where enrollment began. More than half of the men reported that they had consumed five or more alcoholic drinks per episode of drinking in the past month, reported six or more sex partners or had non-condom receptive anal intercourse (ncRAI) with a partner of unknown HIV serostatus in the previous three months. Overall HIV incidence was 3·9/100 person-years (py) in the placebo arm. Only 1% of men reported amphetamine or popper use in the past month.

Table 2 provides results from univariate and multivariate analyses of baseline demographic and risk variables associated with HIV acquisition. Men reporting any ncRAI in the previous three months were more than five times as likely to acquire HIV as men reporting no condomless sex. Among men reporting ncRAI, the hazard was greatest among men reporting this activity with partners believed to be HIV negative (adjusted hazard ratio (AHR) 8·87, 95% confidence interval (CI) 2·29-34·40) or of unknown HIV serostatus (AHR 4·76, 95% CI 1·44-15·71). Only 1% of men reported ncRAI with known HIV positive partners, leading to limited power to assess their risk of HIV acquisition (AHR 7·11, 95% CI 0·70-72·75). One quarter of participants Reported any non-condom insertive anal intercourse (ncIAI) without ncRAI, but this risk factor was not associated with increased HIV acquisition in either univariate or multivariate analysis. Two risk behaviors were significantly associated with HIV acquisition on univariate but not multivariate analysis: cocaine use in the past month, and self-reported STI in the past six months.

The PAF combines data on both the prevalence of risk behaviors and the strength of their association with HIV acquisition to apportion new infections to that risk factor. Overall, ncRAI accounted for 64% of new infections, with a PAF of 53% for ncRAI with partners of unknown serostatus and 10% for ncRAI with HIV negative partners (Table 3). In contrast, the PAF of ncRAI with HIV positive partners was only 1%, likely reflecting the rarity of that practice in this cohort.

The overall NNT (number of persons given PrEP to avoid one infection in one year) is lowest when both the incidence and intervention effectiveness are high for a given subgroup. Overall for the cohort, the NNT was 62 (95% CI 44-147). Figure 3 plots the PAF against the NNT for various subgroups; optimal characteristics would be a high PAF with a low NNT (bottom right corner of the plot), while less favorable characteristics would be a low PAF with a high NNT (upper left corner of the plot). Two risk factors stand out as possessing the desirable qualities of a high PAF and relatively low NNT: men reporting any ncRAI, and specifically those men reporting ncRAI with HIV unknown serostatus partners. Two other factors stand out as having relatively low PAF and a higher NNT than the average: men reporting only one partner, and men reporting ncIAI only, without ncRAI. Having ncRAI with a negative partner, and other sexual and substance use risk had a lower PAF but a relatively low NNT of 60 or less.

Discussion

The simplest and perhaps most effective strategy for identifying MSM/TGW who may benefit most from PrEP would be to ask two questions of men and TGW: In the last three months, have you 1) had sex with men, women, or both; and 2) had anal sex as a bottom without a condom (ncRAI). By offering PrEP to MSM/TGW reporting ncRAI, regardless of partner serostatus, PrEP would be offered to the subgroup of MSM/TGW most likely to benefit from PrEP, based on the results of this analysis.

In our study, ncRAI accounted for nearly 2/3 of new HIV infections, an estimate similar to a recently published study of MSM in Australia, for whom the PAF for ncRAI was 69%.[20] Earlier studies of MSM in the US also found substantial PAF of ncRAI with partners of unknown serostatus[21-22] and ncRAI with partners believed to be HIV negative.[22] That condomless sex with HIV seronegatives (also known as condom serosorting) increases the risk of HIV acquisition compared with consistent condom use is supported by numerous observational studies.[25,26] In fact, the only exception to the risk associated with ncRAI may be for persons in monogamous seroconcordant relationships; in this setting, the risk of HIV acquisition is quite low, even lower than in men who report always using condoms, but have multiple partners.[25]

Conversely, men not reporting condomless anal sex, or only ncIAI, had significantly lower rates of HIV acquisition (1·2 and 1·5/100 py respectively) in our study. These infection rates, while not negligible, are considerably lower than the 2/100 py incidence threshold recommended in some cost effectiveness modeling exercises.[16] Other studies suggest small to moderate PAFs for ncIAI (4-20%),[20,27] with a substantially lower per-contact risk from ncIAI than ncRAI.[28]

A recent model of HIV transmission dynamics among MSM in the US and South America suggests that nearly 40% of new infections among MSM in the US and Peru occur within primary relationships, although only 2/3 of these occur in known serodiscordant relationships.[27] In contrast, in our study, having a known HIV positive partner had a PAF of only 3%. This is likely due in part to the very low prevalence of men entering the study with this risk behavior. Another possible explanation is that the previous models were based on older data, when HIV positive men may have been less likely to receive effective antiretroviral therapy, which may, in turn, reduce their infectiousness.[29] Although no direct data exist on the effectiveness of treatment as prevention for MSM/TGW, providers should surely prioritize offering treatment to the HIV positive member of the couple, both for the patient's own health as well as to reduce the risk of transmission to the uninfected partner.

PrEP may also be offered to the HIV uninfected partner, particularly if the positive partner is not virally suppressed, has sexually transmitted infections, or if the couple engages in condomless sex.

As both cocaine use and self-reporting a sexually transmitted infection had a low NNT in iPrEx, conducting a substance use history and regular STI screening in at-risk MSM/TGW will also identify individuals who may benefit from PrEP. In other MSM cohort studies, amyl nitrite[21] and amphetamines[22] were independently associated with HIV acquisition, with PAFs of 28% and 16% respectively. Use of both substances was low in iPrEx, precluding our ability to evaluate these risks in this study. Similarly, we did not ask about alcohol or substance use before sex, another risk factor with a substantial PAF in other cohorts.[22] The imprecision of self-reported versus diagnosed STIs may also reduce the utility of the former in identifying persons at increased risk. Regardless, either self-reported substance use or STIs should alert the provider to probe more explicitly about sexual risk, and to consider PrEP as part of a larger screening and risk reduction strategy.

These examples demonstrate the challenges providers face in determining to whom to offer PrEP. Clinicians must go beyond considerations of public health benefit to weigh the relative risks against potential benefits for their particular patient in their individual setting. Fortunately, TDF-FTC PrEP has shown few serious adverse effects in clinical trials, although longer follow-up of larger cohorts may be required to detect rare serious events. Renal toxicity was uncommon in HIV uninfected persons, and appeared to be reversible if drugs were stopped during routine monitoring of creatinine.[6,30,31] TDF-FTC appeared to cause a small but statistically significant decrease in bone mineral density,[32] but the clinical significance of this decrease is not clear. Persons with chronic HBV infection may rebound when TDF-FTC PrEP is stopped, and should be monitored; although this rebound has not been seen in trials that enrolled persons with chronic HBV infection.[6,33] Persons with undiagnosed HIV infection who initiate PrEP will likely develop antiretroviral resistance,[6,30,31] which could reduce their treatment options. This emphasizes the importance of regular HIV testing for patients given PrEP, and the need to counsel patients not to re-start PrEP without first being tested for HIV.

There is no explicit threshold for PAF nor NNT to guide clinicians in choosing to whom to offer PrEP. The NNT must be considered by weighing the relative benefit of avoiding HIV infection against the relative dangers of TDF-FTC PrEP for each individual patient.[34,35] Condoms remain one (partially) effective strategy for reducing the risk of HIV acquisition;[7] PrEP offers additional protection that is controlled by the receptive partner. The relative benefits and risks of PrEP should be explicitly discussed with potential PrEP candidates, in the context of other available HIV prevention tools. Potential PrEP users may also factor cost into decisions. At a societal level, discussion may also occur about prioritization of providing PrEP against other health care needs, including provision of antiretroviral therapy for HIV infected persons.[11] Additional cost-effectiveness analyses may be helpful to prioritize how best to reduce new HIV infections in different target populations.

This analysis has several limitations. Although observational data and models suggest similar risk factors for infection among MSM in North and South America,[27] most participants in iPrEx came from the Andean region of South America, and results may not generalize to other regions or persons outside of randomized controlled trials. This analysis also does not apply to PrEP for heterosexual persons, although efficacy has also been demonstrated in this population.[30] The iPrEx trial enrolled relatively few Black MSM in the US or TGW, two populations at particularly high risk of HIV acquisition. The PAFs in this study, although similar in most cases to those from other studies, may have been influenced by the behavioral eligibility criteria for iPrEx. Having condomless anal sex with a known HIV positive partner, although one of the behavioral inclusion criteria, may be considerably less common in geographic regions in which serostatus is often not discussed. Confidence intervals for the PAF and NNT are likely to be relatively large for small subgroups, lending some uncertainty to the estimates. Risk practices are self-reported and may be inaccurate because of social desirability, faulty recall, or desire to meet study eligibility criteria. PrEP effectiveness in clinical settings, and therefore the NNT, could suffer if PrEP adherence is poor, a common weakness among several PrEP trials.[31] Conversely, if high levels of adherence are achieved, such as those seen in the US sites, the NNT will decrease even further. Demonstration projects and studies of innovative, scalable adherence interventions are currently underway.

This analysis suggests that MSM/TGW can be screened for potential eligibility for PrEP even in busy clinical practices by focusing on ncRAI. By adding a few more questions about number and serostatus of sex partners, sexual practices, substance use, and risk reduction strategies, clinicians can gain a broader understanding of patients' needs and formulate a more comprehensive HIV and STI screening and prevention plan. PrEP offers tremendous promise for reducing the spread of HIV globally, but clinicians will need to screen and provide PrEP to at-risk MSM and TGW for PrEP to achieve its promise.

Acknowledgments

Conflicts of interest: AYL has led trials in which study drug was donated by Gilead Sciences and has received personal fees from Clinical Care Options, outside the submitted work. KHM has received unrestricted research and educational grants from Gilead Sciences, and an unrestricted research grant from Merck. PG received an unrestricted grant from Gilead Sciences to develop an educational video related to PrEP. RMG has led trials in which study drug was donated by Gilead Sciences. Gilead Sciences also provided unrestricted travel grants that partially supported annual iPrEx investigator meetings; personal fees from Siemens Healthcare, personal fees from Univ of Pennsylvania, personal fees from ViiV Healthcare, personal fees from Clinical Care Options, personal fees from Kirby Institute (Sydney), personal fees from Medscape Education, outside the submitted work. SPB has led trials in which study drug was donated by Gilead Sciences and has received personal fees from Clinical Care Options, outside the submitted work.

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Research in context

Systematic review

We searched PubMed for published studies of population attributable fraction for HIV infection among MSM/TGW and guidance for offering PrEP to MSM/TGW, using the following search terms: HIV, men who have sex with men, MSM, gay, transgender, population attributable fraction, population attributable risk, pre-exposure prophylaxis, preexposure prophylaxis, PrEP, eligibility, guidelines, guidance, recommendations, providers, physicians, clinicians, number needed to treat, and NNT. We restricted our search to studies published from inception to January 31, 2014.

Interpretation

This is the first study to evaluate clinical trial data to make recommendations about which men who have sex with men and transgender women should be offered PrEP. Current CDC[10] and WHO[11] guidance is not explicit about risk criteria for MSM/TGW to offer PrEP. We combined information about the risk behaviors contributing to new HIV infections and the number of patients per year who would have to be given PrEP to avert one infection. Condomless receptive anal sex with partners of unknown serostatus contributed to more than half of all new HIV infections; similar results have been reported in US[21,22] cohorts. We suggest providers ask a few screening questions of their male and transgender patients and consider offering PrEP to patients with sexual or substance use risk, regardless of knowledge of partner serostatus.

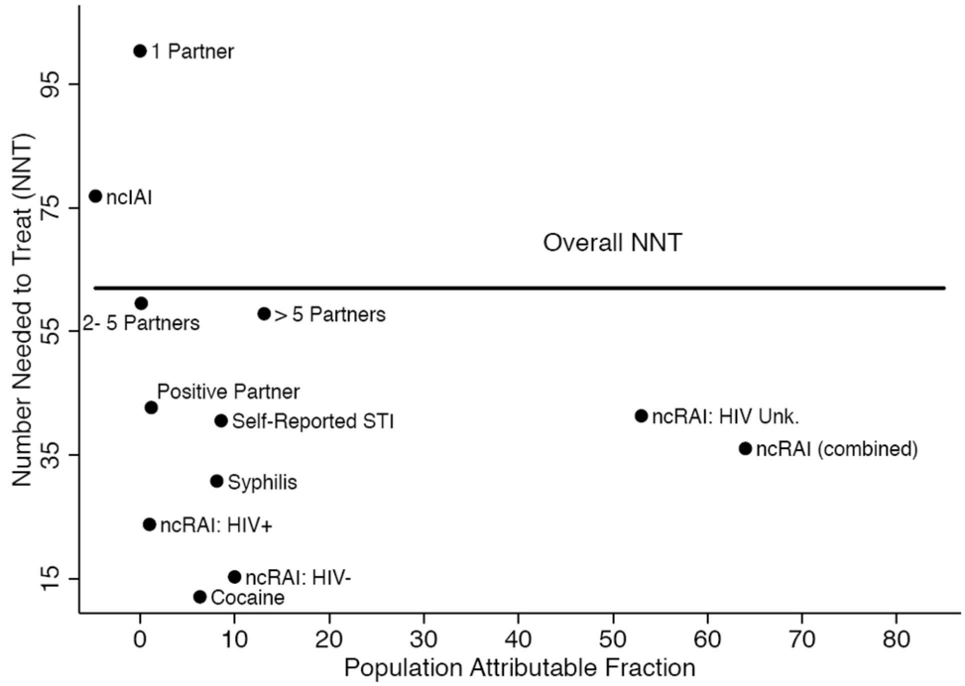

Figure.

The population attributable fraction by the number needed to treat (NNT) per year to prevent one infection in iPrEx. Solid line indicates the average NNT.

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Table 1

Baseline demographic and risk variables associated with HIV infection among placebo recipients in iPrEx

Baseline demographic and risk factors		% of Total N=1248	# Infected N=83	# Uninfected N=1165	Incidence per 100 py
Gender	Male	87%	73	1013	4·0 (3·2, 5·0)
	Transgender male to female	13%	10	152	3·6 (1·9, 6·6)
Age	18-24	53%	47	614	4·3 (3·2, 5·7)
	25-29	19%	15	227	3·7 (2·2, 6·1)
	30-39	18%	19	205	4·8 (3·1, 7·5)
	>= 40	10%	2	119	1·0 (0·2,4·0)
Education[1]	Less than Secondary	20%	16	219	4·0 (2·4, 6·5)
	Secondary	36%	26	417	3·3 (2·2, 4·8)
	Post-Secondary	43%	41	488	4·6 (3·1, 5·1)
Country	Peru	56%	49	651	3·5 (2·7, 4·6)
	Ecuador	12%	17	133	6·5 (4·1, 10·5)
	Brazil	15%	10	174	5·0 (2·7, 9·2)
	United States	9%	2	112	1·3 (0·3, 5·0)
	South Africa	3%	2	41	4·7 (1·1, 19·1)
	Thailand	5%	3	54	5·2 (1·7, 15·9)
Race	Black/African American	8%	6	91	3·0 (1·6, 5·8)
	White	17%	9	200	4·0 (3·2, 5·1)
	Mixed/Other	70%	65	809	4·1 (1·3, 12·7)
	Asian	5%	3	65	3·5 (1·9, 6·5)
Drinking[1,2]	0 Drinks	15%	10	174	3·5 (1·9, 6·5)
	1-4 Drinks per day	28%	29	316	5·0 (3·5, 7·2)
	>= 5 Drinks per day	55%	44	643	3·7 (2·8, 5·0)
Cocaine[2]	None	96%	76	1118	3·7 (3·0, 4·7)
	Any	4%	7	47	9·5 (4·6, 19·7)
HIV+ partner[2]	None	91%	76	1063	3·9 (3·1,4·9)
	Any	9%	7	102	4·4 (2·1, 9·3)
Non-condom position[3]	None	14%	3	175	1·2 (0·4, 3·8)

Baseline demographic and risk factors		% of Total N=1248	# Infected N=83	# Uninfected N=1165	Incidence per 100 py
	ncIAI only	25%	8	309	1·5 (0·7, 2·9)
	Any ncRAI	60%	72	681	5·4 (4·3, 6·9)
ncRAI[3]	None	40%	11	484	1·4 (0·8, 2·5)
	With HIV negative only	5%	9	58	8·9 (4·7, 16·6)
	With unknown serostatus	54%	62	607	5·2 (4·0, 6·6)
	With any HIV positive	1%	1	16	4·3 (0·6, 30·1)
Number of male sex partners[3]	1	8%	5	94	3·4 (1·4, 8·1)
	2-5	37%	26	436	3·4 (2·3, 5·0)
	>5	55%	52	635	4·3 (3·3, 5·7)
Exchange sex[4]	None	59%	49	689	4·1 (3·1, 5·5)
	Any	41%	34	476	3·6 (2·6, 5·1)
STI by self-report[4]	None in prior 6 months	75%	54	878	3·6 (2·7, 4·6)
	Any in prior 6 months	25%	29	287	4·9 (3·4, 7·0)

[1] Missing data on education status for 12 participants and history of alcohol use for 32 participants, none of whom became infected.

[2] Data on drinking and cocaine use in the previous month from CASI

[3] Data on sexual risk in the previous 3 months from interviewer administered questionnaire; ncRAI=non-condom receptive anal intercourse; ncIAI=non-condom insertive anal intercourse

[4] Data on exchange sex and STI self-report in the previous 6 months from CASI

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Table 2

Univariate and multivariate hazard ratios risk of HIV seroconversion by baseline demographic and risk behaviors

Baseline characteristic		Hazard Ratio	95% CI	Adjusted Hazard Ratio	95% CI
Age	18-24	Ref	--		
	25-29	0·88	0·49-1·58		
	30-39	1·13	0·65-1·97		
	>=40	0·26	0·06-10·81		
Education	< Secondary	Ref	--		
	Secondary	1·92	0·45-8·17		
	Post-secondary	2·54	0·60-10·81		
Race	White	Ref	--		
	Black/African American	1·39	0·47-4·12		
	Mixed/other	1·27	0·57-2·82		
	Asian	0·00	0·00-7·69		
Alcohol in past month	None	Ref	--		
	1-4 drinks	1·69	0·82-3·52		
	>= 5 drinks	1·10	0·55-2·22		
Cocaine in past month	Any in past month	2·24	1·01-4·97	1·85	0·81-4·21
HIV positive sex partner*	Any	1·62	0·70-3·75		
Non-condom position	None	Ref	--	Ref	--
	Insertive only	1·56	0·40-6·04	1·68	0·43-6·57
	Any receptive	**5.17**	**1.58-16.94**	**5.11**	**1.55-16.79**
ncRAI by partner serostatus	**Only HIV negative**	**6·69**	**2·69-16·60**	**8·87**	**2·29-34·30**
	Unknown serostatus	**3·56**	**1·85-6·84**	**4·76**	**1·44-15·71**
	Any HIV positive	5·21	0·63-43·21	7·11	0·70-72·75
Number of sex partners*	1	Ref	--		
	2-5	1·27	0·48-3·37		
	>5	1·78	0·66-4·79		
Transactional sex*	Any	0·96	0·60-1·55		

Baseline characteristic		Hazard Ratio	95% CI	Adjusted Hazard Ratio	95% CI
Self-reported STI	Any in past 6 months	1·62	1·01-2·61	1·27	0·76-2·13
Baseline syphilis	Seropositive	1·58	0·92-2·71	1·30	0·73-2·31

* all sexual risk variables cover the 3 months prior to screening

Table 3

Prevalence, population attributable fraction (PAF), efficacy, and number needed to treat (NNT) for subgroups of iPrEx participants, stratified by baseline risk.

Baseline risk behavior		Prevalence	Efficacy	PAF	NNT
Overall		100%	42%	NA	62
Cocaine	Any in last month	4%	87%	6%	12
HIV positive partner*	Any anal sex	9%	63%	1%	43
ncRAI by HIV serostatus*	Only negative	5%	60%	10%	15
	Unknown serostatus	54%	49%	53%	41
	HIV positive	1%	100%	1%	24
Number of partners*	1	8%	36%	0%	100
	2-5	37%	49%	0%	60
	>5	55%	42%	13%	58
Self-reported STI	Any in last 6 months	25%	50%	9%	41

* All sexual risk variables cover the 3 months prior to screening