Published in final edited form as:

AIDS. 2018 January 28; 32(3): 383–392. doi:10.1097/QAD.0000000000001710.

PrEP guidelines have low sensitivity for identifying seroconverters in a sample of Young Black men who have sex with men in Chicago

N Lancki^{1,2}, E Almirol^{1,2}, L Alon^{1,2}, M McNulty¹, and JA Schneider^{1,2}

¹University of Chicago, Department of Medicine, Chicago, IL USA

²Chicago Center for HIV Elimination, Chicago, IL USA

Abstract

Background—Identification of clients at greatest risk of acquiring HIV is critical for PrEP implementation. Young Black men who have sex with men (YBMSM) have high incidence of HIV. We examined published guidelines in identifying eligible PrEP candidates, including seroconverters, in a representative cohort of YBMSM.

Methods—The uConnect cohort included YBMSM aged 16-29 years during PrEP roll-out in Chicago from 2013-2016. YBMSM with indications for PrEP were determined using CDC guidelines, the HIRI-MSM scoring tool, and Gilead recommendations with calculation of sensitivities, specificities and area under the curve (AUC) for HIV seroconversion over 18 months. Incidence Rate Ratios using Poisson regression were modeled to compare individual and network factors associated with seroconversion.

Results—In the study cohort, 300 HIV uninfected YBMSM contributed 390.4 person-years (PY) of follow-up (mean age (SD), 22.3 years (3.07)). HIV incidence was 8.5 cases per 100 PY (95% CI, 6.0-11.9). One network factor was associated with seroconversion: having partners >10 years older (IRR=4.4, 95% CI 1.6-11.8). Overall, 49% of the cohort had an indication for PrEP using CDC guidelines; 72% using HIRI-MSM, and 86% using Gilead recommendations. HIV seroconverters (n=33) were identified as PrEP eligible prior to seroconversion with sensitivities/AUCs for CDC (52%/0.51), HIRI-MSM (85%/0.57) and Gilead guidelines (94%/0.54).

Conclusions—Low sensitivity of CDC guidelines and limited AUC of HIRI-MSM and Gilead screening tools are of concern for PrEP implementation among most at risk populations such as YBMSM. Consideration of demographics, local epidemiology and network factors may better guide identification of clients who could benefit most from PrEP.

Keywords

HIV prevention; Preexposure prophylaxis (PrEP); national guidelines; Young Black men who have sex with men

Corresponding author: John Schneider, MD, MPH, Address: 5837 S. Maryland, L-038 Chicago, IL 60637, Phone: (773) 702-9967, jschnei1@bsd.uchicago.edu.

uConnect Study Team: Ishida Robinson, Eve Zurawski, Elc Estrera, Billy Davis, Dexter Voisin, Steve Muth, Michelle Taylor, Ethan Morgan, Aditya Khanna, Britt Skaathun, Rebecca DuVoisin, Iman Little, Keith Green and Billy Davis.

Introduction

Pre-exposure prophylaxis (PrEP) has the potential to reduce new HIV transmission events [1]. Implementation of PrEP in high risk populations is critical to reducing new HIV infections [2] and achieving National HIV/AIDS Strategy (NHAS) goals in the United States (US). These goals, however, are daunting given the considerable limitations in PrEP awareness and uptake among most at-risk populations such as young Black men who have sex with men (YBMSM). PrEP awareness in several urban epicenters during PrEP implementation has been found to be very low among YBMSM with 40.5% in Chicago [3], 34% in New York [4], and 23% in Atlanta [5]. Much of this has been attributed to individual-level factors including age, race, lack of engagement in health care, and HIV/MSM stigma around PrEP use [5].

In 2014, the Center for Disease Control and Prevention (CDC) issued clinical practice guidelines formulated by an expert panel and data from several clinical trials to support broader implementation of PrEP [6, 7]. In addition to the CDC standard guidelines, guidance has also been provided by the HIV Incidence Risk Index for MSM (HIRI-MSM) screening tool and Gilead's TRUVADA for PrEP package insert. The CDC guidelines for PrEP use by MSM have criteria that include anal sex without condoms, diagnosis with an STI, and being in an ongoing sexual relationship with an HIV-positive male partner [8]. The HIRI-MSM consists of seven questions to assess HIV risk, validated on independent datasets [9, 10] with a score ≥ 10 having a sensitivity of 84% in predicting incident HIV infection [11], and recommended as an indication to evaluate a client for PrEP [8]. Gilead indications for PrEP consideration include individual risk behaviors, as well as engaging in sexual activity in an area or social network of high-prevalence and structural factors, including ever being incarcerated, exchanging sex for commodities, and drug use [12].

In establishing these guidance documents, cohorts of young Black MSM have not been included [6, 7, 9, 10, 13], and analysis has not been conducted during PrEP implementation. Accordingly, we use data from uConnect, a longitudinal cohort of YBMSM 16-29 years of age in Chicago, followed at three time points from 2013-2016. Our objectives for this analysis are to evaluate the sensitivity, specificity, and area under the ROC curve (AUC) of three sets of existing guidelines, to examine individual and network factors associated with HIV seroconversion in this study cohort, and to determine dynamic PrEP awareness and use over this PrEP implementation period.

Methods

Setting

The baseline uConnect sample was generated in 2013 using respondent-driven sampling (RDS). The sampling scheme and sample generation have been described previously [14, 15]. The study includes three time points for data collection: a baseline visit between June 2013 and July 2014 (wave 1) and two follow-up visits, one between April 2014 and May 2015 (wave 2) and another between February 2015 and February 2016 (wave 3). Follow-up visits were conducted 9 months apart over an 18 month period. Each study visit consisted of a structured interview and laboratory testing for HIV and Syphilis infection. This analysis

uses survey responses and HIV testing from the baseline visit and the two follow up visits, hereafter, referred to as wave 1, wave 2, and wave 3, respectively.

Eligibility Criteria

Persons were eligible to participate in the study if they were (1) self-identified as African American or Black, (2) assigned male at birth, (3) between 16 and 29 years of age, (4) reported oral or anal intercourse with a man within the past 24 months, (5) spent most of their time on the South Side of Chicago and (6) willing and able to provide informed consent at the time of the study visit. Participants were included in these analyses if they were HIV-uninfected at wave 1. We excluded participants who were HIV seropositive at wave 1. For participants without blood samples HIV seropositive status was verified by the Chicago Department of Public Health surveillance data following signed release of information. For the seroconversion analysis, we included participants who had documented seroconversion based upon change in serostatus or evidence of acute HIV infection at a follow-up study visit. Participants were included in the PrEP awareness and use analysis if they attended both wave 1 and wave 2 study visits and answered items on PrEP awareness and use at both time points.

Measures

PrEP Eligibility—Survey items from the wave 1 study visit assessing sexual behavior, sexual partner characteristics and other risk factors were used to determine PrEP eligibility according to three sets of guidelines: the CDC's Clinical Practice Guidelines for MSM, the HIV incidence risk index for MSM (HIRI-MSM), and the Gilead indications for PrEP use. CDC's Clinical Practice Guidelines were followed to create a variable to reflect eligibility for PrEP [16]. This was operationalized using a combination of indicators of risk including report of sex with an HIV-infected partner and/or anal sex without condoms or diagnosis of an STI. The HIRI-MSM index was utilized and operationalized using respondent age, number of male partners, number of HIV-infected partners, occurrence of receptive anal intercourse, and use of poppers or amphetamines [8]. Risk scores were computed for respondents and those with a score ≥ 10 were classified as being eligible for PrEP. Gilead PrEP recommendations from the package insert provided PrEP indications for MSM at high risk of HIV acquisition [12]. Eligibility was operationalized using a combination of indicators of risk including report of an HIV-infected partner, and/or engaging in sexual activity in a high prevalence area or social network with at least one of the following: anal sex without condoms, diagnosis of a STI, exchange of sex for commodities, use of illicit drugs or alcohol dependence, incarceration or partner of unknown HIV status. See Supplementary Table 1 for further details on variables used to define PrEP eligibility.

Laboratory testing and determination of acute infection—HIV infection status was determined by three assays applied to dry blood spot samples: ARCHITECT HIV Ag/Ab Combo, Multispot HIV-1/HIV-2 Bio-Rad, and Realtime HIV-1 RNA (Abbot). All samples collected included testing for HIV-1 RNA. Acute infection was documented in cases where viral load was detectable and 4th/3rd generation tests were negative. We compared HIV serostatus at each study wave using laboratory test results from the wave 1, wave 2 and wave

3 visits; participants who tested negative at the wave 1 visit and had a seropositive result or who were acutely infected at a subsequent visit were classified as seroconverters.

Person-Time for HIV incidence—For participants who remained HIV-negative throughout follow-up, we calculated their person-time as the difference between the date of the last study visit they attended (wave 2 or wave 3) and the date of the wave 1 study visit. For HIV seroconverters, we defined the date of seroconversion as halfway between the first visit when HIV was diagnosed and the previous visit. We assessed sociodemographic, behavioral, structural and network factors associated with incident HIV during the study period, in order to evaluate what YBMSM client-level factors may improve existing PrEP guidelines.

PrEP Awareness and Use—PrEP awareness was self-reported by respondents: “PrEP (pre-exposure prophylaxis) is when a person is given medicine before being exposed to HIV (like when they expect that they will be having unprotected sex with an infected partner) to prevent them from becoming infected. Before today, have you heard of PrEP?” This question was asked at wave 1 (June 2013 – July 2014) and wave 2 (April 2014– May 2015). Those respondents who reported having heard of PrEP were subsequently asked if they had ever used PrEP. Participants who were aware of PrEP at wave 1 and/or wave 2 were categorized as “PrEP aware”; those who were unaware at both wave 1 and wave 2 were categorized as “Persistently unaware”. Active PrEP linkage services became available in wave three of the study at which time all participants were provided detailed information on PrEP and offered linkage to PrEP care regardless of insurance status or ability to pay.

Statistical Analysis

Gile's Sequential Sampling (SS) estimator was utilized to weight our population-based sample and generate probability estimates [17]. Weights were generated in Stata 14 [18]. To assess the performance of the different criteria in identifying respondents who were at increased risk for seroconversion, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC) for the three PrEP eligibility criteria were calculated. Incidence-density rates and weighted bivariate and multivariate rate-ratios (RR) were computed for incident HIV infection over the study period, and sociodemographic, behavioral and network factors associated with HIV seroconversion were determined using Poisson regression models. A sensitivity analysis was performed excluding participants who reported ever having used PrEP. Wave 1 characteristics of respondents were summarized and compared by PrEP awareness over the first two waves of the study using chi-square and t-tests for categorical and continuous variables, respectively. Differences in eligibility by PrEP use and PrEP awareness were also compared using chi-square and t-tests. Bivariate and multivariate logistic regression models were implemented to examine factors associated with PrEP awareness and use over the study period. All statistical analyses were performed in Stata 14.1 [18].

Results

Study Cohort

Among 618 participants who completed the Wave 1 interview of the study, more than one-third (n=225, 37.0%) of participants were HIV seropositive, and 52 (23.1%) were previously unaware of their infection. Of the remaining 393 participants, 343 had a documented negative HIV test at wave 1. Participants who did not have a documented HIV negative test from cohort labs or CDPH surveillance data were excluded from analyses (n=50). Cumulative retention over the study period was 87% (n=300) (see Figure 1); these individuals represented the final study sample for the seroconversion analysis. The final study sample for the PrEP awareness and use analysis consisted of participants who answered questions about PrEP awareness and use at the wave 2 study visit (n=288).

Indications for PrEP

Approximately half of the sample (49%) met criteria for PrEP use according to CDC guidelines, 72% according to HIRI-MSM Risk Index, and 86% met the Gilead indications for PrEP. Figure 2 shows the proportion of YBMSM eligible for PrEP according to the three guidelines by PrEP awareness, PrEP use, and seroconversion, respectively.

Performance of Screening Guidelines

During the two year follow up, 33 incident infections were observed over 390.4 person-years for an incidence rate of 8.5 per 100 person-years (95% CI: 6.0 to 11.9 per 100 PY). The sensitivity, specificity, positive predictive values (PPV), and area under the ROC curve (AUC) for the three guidelines in identifying participants at risk for seroconversion are shown in Figure 3. The CDC guidelines were associated with a sensitivity of 52% (i.e., of those who became infected during the study period, 52% were eligible for PrEP by CDC guidelines), a specificity of 52% and an AUC of 0.51. The HIRI-MSM Score 10 was associated with a 85% sensitivity, 30% specificity, and an AUC of 0.54. The Gilead Guidelines were associated with a 94% sensitivity, 15% specificity, and an AUC of 0.57. The weighted sensitivity/specificity estimates were: CDC guidelines (30%/59%), HIRI-MSM risk score (93%/22%), and Gilead guidelines (76%/36%).

Factors Associated with HIV Seroconversion

Table 1 provides weighted bivariate analyses of sociodemographic, behavioral, structural, and network factors associated with incident HIV during the study period. Individual level risk factors associated with HIV seroconversion included being unemployed versus employed full time (IRR=3.8, 95% CI 1.2-11.5), having no health insurance (IRR=2.4, 95% CI 1.0-5.7), having an anorectal STI test performed in the past 2 years (IRR= 3.3, 95% CI 1.3-8.5) and popper use (IRR=3.3, 95% CI=3.3 (1.0, 10.7). Having any partners 10 years older was a network level predictor of HIV incidence (IRR=4.4, 95% CI 1.6-11.8). In multivariate analyses adjusting for age and sexual identity, having any partners 10 years older remained a significant predictor of seroconversion (aIRR 4.6, 95% CI 1.9, 11.0, p=0.001). The results did not change significantly after performing a sensitivity analysis excluding participants who reported ever having used PrEP. Popper use (IRR=4.2, 95% CI

1.3-14.0, $p=0.022$) remained an individual level factor associated with HIV seroconversion, while having no health insurance (IRR=2.2, 95% CI 0.9-5.5, $p=0.099$) and being unemployed versus employed full time (IRR=2.7, 95% CI 1.0-7.2, $p=0.005$) became marginally significant. Having an anorectal STI test performed in the past 2 years (IRR=2.4, 95% CI 0.8-7.2, $p=0.118$) was no longer predictive. Having any partner 10 years older remained a network level risk factor (IRR=3.9, 95% CI 1.5-10.3, $p=0.006$). The HIRI-MSM Index (IRR=3.2, 95% CI 1.0-10.1, $p=0.052$) was marginally significantly associated with HIV incidence in the sensitivity analysis.

Alternative Guideline Thresholds

We explored alternative thresholds for the HIRI-MSM Risk Index to determine if a different cut-off score would be optimal in this population. At a cutoff of 8, sensitivity increased from 85% to 91%, but specificity and AUC decreased (11% and 0.51, respectively). The ROC curve and sensitivity/specificity at different cut-offs are shown in Supplemental Table 2 and the Supplemental Figure 1. Adding having a partner 10 years to the CDC criteria resulted in better performance of the CDC guidelines, with AUC=0.61, sensitivity=69%, and specificity=52% (vs current sensitivity of 52%, specificity 52%, and AUC=0.51).

PrEP Awareness and Use

PrEP awareness increased from 32% to 64% from 2013-2015; 36% of participants were persistently unaware of PrEP over this time period. Table 2 demonstrates bivariate comparisons of participant characteristics from the wave 1 visit by dynamic PrEP awareness over the first two study waves. In the weighted multivariable regression model, participants were less likely to be aware of PrEP if they identified as bisexual versus gay (aOR=0.33, 95% CI 0.19-0.58, $p<0.001$) or reported being very close to the black community (aOR=0.56, 95% CI 0.32, 0.972, $p=0.041$). Ever having participated in an HIV prevention program (aOR= 2.85; 95% CI 1.40-5.78, $p=0.004$) and having a higher proportion of social network members who were HIV positive (for every 10% increase: aOR= 1.26, 95% CI 1.01-1.57, $p=0.041$) were positively associated with being PrEP aware.

Self-reported PrEP use increased slightly over the study period, but remained low, from 4% at wave 1 to 6.6% at wave 2 and 10.1% by wave three. Factors associated with PrEP use included having an STI diagnosed in the past 12 months (OR=2.29; 95% CI 1.10-4.80, $p=0.027$), having an HIV positive partner (OR=4.23, 95% CI 1.78-10.07, $p=0.001$), and having a partner of unknown HIV status (OR=2.31; 95% CI=1.15-4.65, $p=0.019$).

Discussion

This is the first study to evaluate the performance of existing PrEP guidelines in a cohort of YBMSM and provides important information to consider when determining PrEP eligibility. Accordingly, there are several important findings from this analysis. First, in the context of high HIV seroconversion rates with an incidence of 8.5 cases per 100 person-years, we identified one network predictor of seroconversion: having any sex partners 10 years older in this population. Certainly, this specific predictor may be helpful in refining future versions of PrEP guidelines. Most important to updating PrEP recommendations is our finding that

nearly half of seroconverters would not have been eligible for PrEP according to CDC guidelines, the guidelines most often used by physicians in prescribing PrEP [19, 20]. While the Gilead guidelines had high sensitivity and the best AUC (although marginally), low specificity, and positive predictive values were evident across the three different guidelines.

Overall, our findings were consistent with other studies demonstrating that BMSM were less likely to meet indications for PrEP compared to other racial groups, despite their acute risk for HIV acquisition [21, 22]. Low eligibility rates and lack of association between behavioral risks and seroconversion may be race specific. CDC guidelines are based on randomized controlled trials, which included predominantly white MSM [23]; these trials had limited numbers of BMSM in the study populations [1, 9, 10]. Studies have found seroadaptive behaviors that are protective for White MSM do not necessarily appear to be protective in Black MSM [24]. Sullivan et al. identified factors involved in HIV seroconversion among Black and White MSM from data collected within a cohort study in Atlanta initiated in 2010. Their data demonstrated that PrEP eligibility guidelines based on individual-level behaviors are likely to underestimate the risk for Black MSM, with only 65% of seroconverters meeting eligibility guidelines [22]. Their study also identified two network factors to be significant predictors of incident HIV infection: having a partner 10 years older and the race of the partner. Similarly, our analyses found that having a partner 10 years older to be associated with HIV seroconversion. Notably in our cohort, important attributes unique to YBMSM (i.e. membership in house/ball community, criminal justice involvement) were not major HIV incidence predictors. Findings that many of the individual risk factors used in guidelines are not predictive of YBMSM seroconversion, indicate the need for more nuanced and locally relevant guidelines for PrEP use. Alternative guidelines that take into account network or other population level factors may be more effective in guiding physicians and in turn preventing HIV in these communities.

Complicating the HIV prevention potential of PrEP was the relatively low level of PrEP awareness among this representative sample of YBMSM and concomitantly, the low level of PrEP use. The level of overall PrEP awareness increased over the study period in this cohort; however, one-third of study participants had never heard of PrEP and 10.1% had ever used PrEP three years following FDA approval when providers in Chicago started first providing PrEP to patients [25]. While some components of the guidelines (i.e. HIV positive partner, STI diagnosis) were associated with PrEP use, PrEP use was not associated with overall eligibility by the guidelines, with only 10% of clients meeting CDC guidelines ever using PrEP. As demonstrated in previous work [3], PrEP awareness is associated with variables that indicate some level of engagement in HIV programming or in health care systems generally. Other studies have indicated that PrEP knowledge is associated with health care engagement such as experiencing recent HIV testing [5, 26] or having had an STI diagnosed in clinic [27]. Increased engagement of YBMSM in HIV programming or health-care will likely increase PrEP awareness and use in this population.

In addition to potential individual-level factors, provider-level barriers to PrEP initiation also likely exist. Karris et al. found significant variation in infectious disease physician attitudes and practices around PrEP, which may in part explain the lack of association between PrEP eligibility and use [28]. Other studies have demonstrated low levels of PrEP prescribing,

particularly for young men of color. In one study, healthcare providers were more likely to believe prescribing PrEP would increase risk behaviors in BMSM than their white counterparts, resulting in decreased willingness to prescribe PrEP [29]. In the current analysis, we did not identify reasons for low PrEP use, and it remains unclear to what extent providers are contributing to limited awareness and uptake among YBMSM.

Our study had some important limitations. We used wave 1 factors to define indications for PrEP; however, an individual may have engaged in varied risk behaviors between study visits and behaviors may have changed over the 18 month study period. In addition, some of the questions used to operationalize PrEP indications were for the previous 12 months instead of in the previous six months, as most of the CDC guidelines outline. This, however, would likely result in an overestimate of those who were eligible from our study sample and result in reduced specificity. All models were estimated with and without the RDS sampling weights. Our conclusions and main findings were unchanged using the weighted and unweighted models. However, there was a relatively large discrepancy between the weighted and unweighted sensitivity for the CDC guidelines (30% versus 52%). The RDS weights were derived under a number of assumptions relating to RDS that have been described previously [3, 15, 30]. We believe the RDS assumptions were met, however, both weighted and unweighted estimates are presented for sensitivity, specificity, and PPV. Some participants only attended the wave 2 follow-up visit and did not have as much time to acquire HIV and be observed. If loss to follow-up was related to the predictors or seroconversion, these results may be biased. Finally, we had relatively small numbers of incident outcomes to evaluate predictors of seroconversion and PrEP use in the study cohort.

Having a standardized, effective PrEP eligibility decision aid for HIV vulnerable populations such as YBMSM may assist with PrEP implementation efforts. In 2014, the World Health Organization (WHO) recommended offering PrEP to populations with an HIV incidence of about three per 100 person-years or higher [31]. In our cohort, the incidence rate was 8.5 cases per 100 person-years. Public health programs and health care providers should consider demographics, local epidemiology, and network factors when considering provision of PrEP to patients. Additional efforts to better understand these networks may help further target prevention strategies [32].

In summary, we have demonstrated that several client-level factors listed in existing guidelines to determine PrEP eligibility may exclude a substantial proportion of most-at-risk-persons who could benefit from PrEP in the United States. PrEP with its demonstrated efficacy is susceptible to implementation failure and concerted efforts should be made to increase awareness and use among those at highest risk for HIV. We recommend that all YBMSM in high prevalence areas should be initially offered PrEP regardless of self-reported risk behaviors, with continued follow-up and shared decision making [33] around when PrEP cessation should occur.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by NIH grants R01DA033875, R01 DA039934 and R01AI120700. We would also like to thank all study participants for the time and effort required to recruit their network members and take part in the interview.

References

1. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010; 363:2587–2599. [PubMed: 21091279]
2. Kelley CF, Kahle E, Siegler A, Sanchez T, Del Rio C, Sullivan PS, et al. Applying a PrEP Continuum of Care for Men Who Have Sex With Men in Atlanta, Georgia. *Clin Infect Dis*. 2015; 61:1590–1597. [PubMed: 26270691]
3. Khanna AS, Michaels S, Skaathun B, Morgan E, Green K, Young L, et al. Preexposure Prophylaxis Awareness and Use in a Population-Based Sample of Young Black Men Who Have Sex With Men. *JAMA Intern Med*. 2016; 176:136–138. [PubMed: 26571368]
4. Gupta S, Lounsbury DW, Patel VV. Low Awareness and Use of Preexposure Prophylaxis in a Diverse Online Sample of Men Who Have Sex With Men in New York City. *J Assoc Nurses AIDS Care*. 2016
5. Eaton LA, Driffin DD, Bauermeister J, Smith H, Conway-Washington C. Minimal Awareness and Stalled Uptake of Pre-Exposure Prophylaxis (PrEP) Among at Risk, HIV-Negative, Black Men Who Have Sex with Men. *AIDS Patient Care STDS*. 2015; 29:423–429. [PubMed: 26083143]
6. Pinkerton SD, Abramson PR. Effectiveness of condoms in preventing HIV transmission. *Soc Sci Med*. 1997; 44:1303–1312. [PubMed: 9141163]
7. Menza TW, Hughes JP, Celum CL, Golden MR. Prediction of HIV acquisition among men who have sex with men. *Sex Transm Dis*. 2009; 36:547–555. [PubMed: 19707108]
8. US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2014 Clinical Providers' Supplement. 2014
9. Bartholow BN, Buchbinder S, Celum C, Goli V, Koblin B, Para M, et al. HIV sexual risk behavior over 36 months of follow-up in the world's first HIV vaccine efficacy trial. *J Acquir Immune Defic Syndr*. 2005; 39:90–101. [PubMed: 15851919]
10. Koblin B, Chesney M, Coates T, Team ES. Team ES. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet*. 2004; 364:41–50. [PubMed: 15234855]
11. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2012; 60:421–427. [PubMed: 22487585]
12. Gilead Sciences Inc. TRUVADA [package insert]. Foster City, CA: 2013.
13. Flynn NM, Forthal DN, Harro CD, Judson FN, Mayer KH, Para MF, et al. Placebo-controlled phase 3 trial of a recombinant glycoprotein 120 vaccine to prevent HIV-1 infection. *J Infect Dis*. 2005; 191:654–665. [PubMed: 15688278]
14. Morgan E, Skaathun B, Michaels S, Young L, Khanna A, Friedman SR, et al. Marijuana Use as a Sex-Drug is Associated with HIV Risk Among Black MSM and Their Network. *AIDS Behav*. 2015
15. Schneider J, Cornwell B, Jonas A, Lancki N, Behler R, Skaathun B, et al. Network dynamics of HIV risk and prevention in a population-based cohort of young Black men who have sex with men. *Network Science*. 2017; 5:381–409.
16. Department of Health and Human Services. , editor. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States: 2014 clinical practice guideline. Atlanta: 2014.
17. Gile K. Improved Inference for Respondent-Driven Sampling Data with Application to HIV Prevalence Estimation. *Journal of the American Statistical Association*. 2011; 106:135–146.
18. StataCorp. Stata: Release 14 Statistical Software. College Station, TX: StataCorp LP; 2015.

19. Calabrese SK, Magnus M, Mayer KH, Krakower DS, Eldahan AI, Gaston Hawkins LA, et al. Putting PrEP into Practice: Lessons Learned from Early-Adopting U.S. Providers' Firsthand Experiences Providing HIV Pre-Exposure Prophylaxis and Associated Care. *PLoS One*. 2016; 11:e0157324. [PubMed: 27304883]
20. Smith DK, Mendoza MC, Stryker JE, Rose CE. PrEP Awareness and Attitudes in a National Survey of Primary Care Clinicians in the United States, 2009-2015. *PLoS One*. 2016; 11:e0156592. [PubMed: 27258374]
21. Hoots BE, Finlayson T, Nerlander L, Paz-Bailey G. National HIVBSSG. Willingness to Take, Use of, and Indications for Pre-exposure Prophylaxis Among Men Who Have Sex With Men-20 US Cities, 2014. *Clin Infect Dis*. 2016; 63:672–677. [PubMed: 27282710]
22. Sullivan PS, Rosenberg ES, Sanchez TH, Kelley CF, Luisi N, Cooper HL, et al. Explaining racial disparities in HIV incidence in black and white men who have sex with men in Atlanta, GA: a prospective observational cohort study. *Ann Epidemiol*. 2015; 25:445–454. [PubMed: 25911980]
23. Schneider JA, Bouris A, Smith DK. Race and the Public Health Impact Potential of Pre-Exposure Prophylaxis in the United States. *J Acquir Immune Defic Syndr*. 2015; 70:e30–32. [PubMed: 25950209]
24. Golden MR, Dombrowski JC, Kerani RP, Stekler JD. Failure of serosorting to protect African American men who have sex with men from HIV infection. *Sex Transm Dis*. 2012; 39:659–664. [PubMed: 22902660]
25. Food US. Drug Administration. Truvada for PrEP Fact Sheet: Ensuring Safe and Proper Use. 2012
26. Rucinski KB, Mensah NP, Sepkowitz KA, Cutler BH, Sweeney MM, Myers JE. Knowledge and use of pre-exposure prophylaxis among an online sample of young men who have sex with men in New York City. *AIDS Behav*. 2013; 17:2180–2184. [PubMed: 23479003]
27. Dolezal C, Frasca T, Giguere R, Ibitoye M, Cranston RD, Febo I, et al. Awareness of Post-Exposure Prophylaxis (PEP) and Pre-Exposure Prophylaxis (PrEP) Is Low but Interest Is High Among Men Engaging in Condomless Anal Sex With Men in Boston, Pittsburgh, and San Juan. *AIDS Educ Prev*. 2015; 27:289–297. [PubMed: 26241380]
28. Karris MY, Beekmann SE, Mehta SR, Anderson CM, Polgreen PM. Are we prepped for preexposure prophylaxis (PrEP)? Provider opinions on the real-world use of PrEP in the United States and Canada. *Clin Infect Dis*. 2014; 58:704–712. [PubMed: 24319083]
29. Calabrese SK, Earnshaw VA, Underhill K, Hansen NB, Dovidio JF. The impact of patient race on clinical decisions related to prescribing HIV pre-exposure prophylaxis (PrEP): assumptions about sexual risk compensation and implications for access. *AIDS Behav*. 2014; 18:226–240. [PubMed: 24366572]
30. Gile KJ, Handcock MS. Respondent-Driven Sampling: An Assessment of Current Methodology. *Sociological Methodology*, Vol 40. 2010; 40:285–327.
31. World Health Organization. Policy Brief PrEP. 2015.
32. Schneider JAC, B Jonas A, Behler R, Lancki N, Skaathun B, Michaels S, Khanna AS, Young LE, Morgan E, Duvoisin R, Friedman S, Schumm P, Laumann EO. Network dynamics and HIV risk and prevention in a population-based cohort of Young Black Men Who have Sex with Men. *Network Science*. In press.
33. Peek ME, Lopez FY, Williams HS, Xu LJ, McNulty MC, Acree ME, et al. Development of a Conceptual Framework for Understanding Shared Decision making Among African-American LGBT Patients and their Clinicians. *J Gen Intern Med*. 2016; 31:677–687. [PubMed: 27008649]

Figure 1. uConnect Population with Inclusion and Exclusion Criteria

Figure 2. PrEP Eligibility by Awareness, Use, and Seroconversion with uConnect Chicago cohort from 2013-2016

Figure 3.
 Sensitivity, specificity, AUC and PPV of existing PrEP Guidelines (N=300)

Table 1
Predictors of incident HIV infection among YBMSM in uConnect cohort, Chicago, 2013-2016 (N=300)

Characteristic	HIV infections	Person-years (PY)	Incidence rate per 100 PY (95% CI)	Incidence rate ratio (95% CI) ^a
Overall	33	390.4	8.5 (6.0, 11.9)	-
Sociodemographic and clinical				
Age, years				
18-24	28 (84.8)	298.0	9.4 (6.5, 13.6)	2.5 (0.7, 8.3)
25	5 (15.2)	92.4	5.4 (2.3, 13.0)	<i>ref</i>
Sexual identity				
Gay	21 (65.6)	241.1	8.7 (5.7, 13.4)	<i>ref</i>
Bisexual	7 (21.9)	131.7	5.3 (2.5, 11.2)	0.7 (0.2, 2.2)
Straight/something else	4 (12.5)	17.4	23.0 (8.6, 61.3)	3.5 (0.6, 19.3)
Education				
High school (HS) or GED, or less	7 (24.1)	116.4	6.0 (2.9, 12.6)	<i>ref</i>
Some college, Associates or technical school	21 (72.4)	215.2	9.8 (6.4, 15.0)	1.7 (0.7, 4.2)
College graduate or post-baccalaureate	1 (3.4)	27.5	3.6 (0.5, 25.8)	0.3 (0.05, 2.4)
Employed				
Full time	5 (15.2)	114.5	4.4 (1.8, 10.5)	<i>ref</i>
Part time	9 (27.3)	108.1	8.3 (4.3, 16.0)	2.0 (0.6, 6.9)
Unemployed	19 (57.6)	167.9	11.3 (7.2, 17.7)	3.8 (1.2, 11.5) *
No health insurance	18 (62.1)	205.1	6.3 (3.5, 11.4)	2.4 (1.0, 5.7) *
Unstably housed	7 (21.2)	293.1	7.2 (3.5, 15.2)	0.5 (0.2, 1.4)
Ever in jail	12 (39.4)	168.3	7.1 (4.0, 12.6)	0.6 (0.3, 1.3)
Anorectal STI test performed in past 2 years	10 (30.3)	92.4	10.8 (5.8, 20.1)	3.3 (1.3, 8.5) *
Sexual behaviors				
Any main partner	13 (36.4)	148.9	8.7 (5.1, 15.0)	1.1 (0.4, 2.7)
Any condomless sex	19 (57.6)	203.8	9.3 (5.9, 14.6)	0.7 (0.3, 1.6)
Exchanged sex ^b	0 (0)	36.1	0 (0)	-
Group sex in past 12 months	8 (24.2)	53.6	14.9 (7.5, 29.9)	1.3 (0.5, 3.7)
Drug use				
Any drug use ^c	17 (51.5)	187.1	9.1 (5.6, 14.6)	1.2 (0.5, 2.7)
Marijuana use	27 (81.8)	284.9	9.5 (6.5, 13.8)	1.3 (0.4, 4.3)
Methamphetamine use	0 (0)	1.3	0 (0)	-
Poppers use	4 (12.1)	17.9	22.4 (8.4, 59.6)	3.3 (1.0, 10.7) **
Sexual network				
Any partners HIV +	1 (3.0)	39.9	2.5 (0.4, 17.8)	0.3 (0.04, 2.7)
Partner with unknown HIV status	11 (33.3)	91.9	12.0 (6.6, 21.6)	2.8 (1.0, 8.0) †

Characteristic	HIV infections	Person-years (PY)	Incidence rate per 100 PY (95% CI)	Incidence rate ratio (95% CI) ^a
Any partner 10 years older	10 (30.3)	65.9	15.2 (8.2, 28.2)	4.4 (1.6, 11.8) *
Any partners in jail	16 (48.5)	169	9.5 (5.8, 15.5)	1.2 (0.6, 2.6)
Any sex drug use with partner	17 (51.5)	162.9	10.4 (6.5, 16.8)	1.1 (0.5, 2.5)
Any race mixing	4 (12.1)	56.3	7.1 (2.7, 18.9)	1.2 (0.2, 6.7)
Social Network				
Any network members HIV positive	4 (12.1)	53.0	7.5 (2.8, 20.1)	0.5 (0.2, 1.7)
Any network members in jail	16 (48.5)	198.0	8.1 (5.0, 13.2)	1.0 (0.4, 2.4)
Any network members who use illicit drugs	21 (63.6)	230.5	9.1 (5.9, 14.0)	1.1 (0.5, 2.7)
Close to the Black community	15 (46.9)	185.4	8.1 (4.9, 13.4)	1.0 (0.7, 1.6)
Close to the gay community	8 (24.2)	99.4	8.6 (5.8, 12.7)	1.2 (0.8, 1.8)
House/ball/gay family membership	11 (33.3)	117.9	9.3 (5.2, 16.8)	0.8 (0.4, 1.8)
PrEP Use, Awareness, Eligibility				
PrEP Aware (at either wave)	22 (66.7)	257.5	8.3 (4.6, 14.9)	1.0 (0.4, 2.4)
PrEP Use (any vs none)	4 (12.5)	54.7	7.3 (2.7, 19.5)	1.9 (0.6, 5.8)
Eligibility by guidelines				
CDC guidelines	17 (51.5)	195.1	8.7 (5.4, 14.0)	0.6 (0.3, 1.4)
HIRI-MSM Risk Index	28 (84.8)	277.4	10.1 (7.0, 14.6)	1.6 (0.5, 5.4)
Gilead guidelines	31 (93.9)	332.0	9.3 (6.5, 13.3)	3.3 (0.7, 16.1)

^aWeighted using Giles Sequential Sampling

^bExchanged sex for drugs, goods, other benefits

^cPoppers, cocaine/crack, heroin, psychedelics, methamphetamine, prescription pain killers

[†]p < .10

* p < .05,

** p < .01

Table 2
Characteristics of HIV negative uConnect participants at Wave 1 by dynamic PrEP awareness, Chicago, 2013-2016 (N=288)

Characteristics	Total (n=288)	Persistently unaware (n=103)	PrEP aware (n=185)	P value *
Sociodemographic				
Age years (SD)	22.1 (0.3)	21.7 (0.4)	22.6 (0.3)	0.02
Income <\$20K	83.0	85.8	80.6	0.32
Education HS or less	33.0	29.6	35.0	0.56
Unemployed	26.3	24.9	27.2	0.19
Housing instability	24.9	21.9	26.8	0.65
Criminal justice involvement	36.3	37.8	35.3	0.75
Health care coverage	49.9	55.3	46.5	0.26
Gender				
Male	91.2	95.4	88.5	0.07
Transgender	8.8	4.6	11.6	
Sexual orientation				
Gay	56.3	44.7	63.8	
Bisexual	37.5	53.3	27.3	<.01
Straight/something else	6.2	2.1	8.9	
Clinical				
Has primary health care provider	43.9	50.4	39.9	0.13
Mental health provider	21.2	18.9	22.8	0.38
Participated in an HIV program	25.9	14.0	33.4	0.01
Conversation with HIV outreach worker	33.1	22.8	39.4	<.01
Previous STI diagnosis	13.6	8.8	16.7	0.06
Syphilis seropositive	18.5	23.3	15.4	0.09
Anorectal STI exam performed in past 2 years	20.6	14.9	24.2	0.15
Social				
Uses websites, apps or phone lines to meet/socialize with other men	44.6	43.7	45.2	0.77
House/Ball/Gay Family membership	22.8	18.4	25.6	0.26
Number of BMSM known	4.4 (0.2)	3.8 (0.2)	4.8 (0.3)	0.03
Very close to black community	47.9	57.4	41.6	0.01
Very close to gay community	17.3	16.9	17.6	0.89
Social network				
Degree ***	2.6 (0.1)	2.5 (0.2)	2.6 (.1)	0.74
Proportion HIV positive	5.6 (1.8)	1.0 (0.5)	9.1 (2.9)	0.01
Proportion in jail	30.4 (3.5)	25.2 (4.0)	30.4 (3.5)	0.39
Proportion ever use drugs	41.3 (3.4)	44.6 (6.9)	38.2 (4.3)	0.46
Proportion with group sex	14.5 (1.6)	15.5 (1.7)	14.2 (2.8)	0.66

Characteristics	Total (n=288)	Persistently unaware (n=103)	PrEP aware (n=185)	P value [*]
Proportion family [†]	0.27 (0.02)	0.34 (0.04)	0.23 (0.03)	0.06
Proportion network who know you have sex with men	0.89 (0.02)	0.83 (0.05)	0.92 (0.03)	0.09
Sexual network				
Number of partners in past 6 months, median (IQR)	4.6 (14.8)	2.4 (3.4)	5.3 (18.3)	0.3
Degree ^{***}	2.4 (0.1)	2.4 (0.1)	2.4 (.1)	0.91
Proportion HIV positive	5.7 (1.9)	3.0 (2.2)	8.2 (2.9)	0.13
Proportion in jail	26.8 (2.8)	24.1 (3.4)	29.4 (3.8)	0.26
Proportion ever use drugs	30.9 (3.7)	35.2 (4.7)	28.0 (4.4)	0.14
Proportion with group sex	23.6 (3.7)	21.6 (4.2)	24.7 (4.5)	0.56
Seroconversion	9.2	9.1	9.3	0.95

^{*} Weighted using Giles Sequential Sampling

^{**} Chi-square or Fisher's exact test used for categorical variables, t-test or Wilcoxon test used for continuous variables

^{***} The proportion of social network that are family (defined as parent, child/stepchild, sibling, in-law or other relative).

[†] Number of network members named