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Are CDC Guidelines for Pre-Exposure Prophylaxis Specific Enough? Formulation of a Personalized HIV Risk Score for Pre-Exposure Prophylaxis Initiation

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Abstract

Background—Pre-exposure prophylaxis (PrEP) has emerged as an HIV prevention tool for populations at highest risk for HIV infection. Current CDC guidelines for identifying PrEP candidates may not be specific enough to identify gay, bisexual, and other men who have sex with men (MSM) at the highest risk for HIV infection. We created an HIV risk score for HIV-negative MSM based on Syndemics Theory to develop a more targeted criterion for assessing PrEP candidacy.

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Conflicts of Interest

None declared for any authors.

COMPLIANCE WITH ETHICAL STANDARDS

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

A waiver of informed consent was obtained from the IRB for all participants included in the study due to the study's retrospective design. Specifically, this study was approved by the University of California, Los Angeles South General Institutional Review Board #5 (IRB00004474; Project No. 14-000982).

Methods—Behavioral risk assessment and HIV testing data were analyzed for HIV-negative MSM attending the Los Angeles LGBT Center between January 2009 and June 2014 (n = 9,481). Syndemics Theory informed the selection of variables for a multivariable Cox proportional hazards model. Estimated coefficients were summed to create an HIV risk score, and model fit was compared between our model and CDC guidelines using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC).

Results—Approximately 51% of MSM were above a cut-point that we chose as an illustrative risk score to qualify for PrEP, identifying 75% of all seroconverting MSM. Our model demonstrated a better overall fit when compared to the CDC guidelines (AIC Difference = 68) in addition to identifying a greater proportion of HIV infections.

Conclusions—Current CDC PrEP guidelines should be expanded to incorporate substance use, partner-level, and other Syndemic variables that have been shown to contribute to HIV acquisition. Deployment of such personalized algorithms may better hone PrEP criteria and allow providers and their patients to make a more informed decision prior to PrEP use.

Keywords

Men who Have Sex with Men; HIV; Pre-exposure Prophylaxis; Syndemics Theory; Time to Event Data; Hazard Ratio

INTRODUCTION

Gay, bisexual, and other men who have sex with men (MSM) account for over 60% of all new HIV cases annually in the United States (1). While prevention efforts originally relied on frequent testing and early treatment of HIV, the prophylactic use of antiretroviral drugs now shows promise in decreasing HIV burden in this population.

In 2012, the US Food and Drug Administration approved tenofovir disoproxilemtricitabine (Truvada®), an antiretroviral medication, as pre-exposure prophylaxis (PrEP), for daily dosing by high-risk HIV-negative individuals to prevent HIV infection. The US Centers for Disease Control and Prevention (CDC) state that PrEP is appropriate for "[a] gay or bisexual man who has had anal sex without a condom or [has] been diagnosed with a [sexually transmitted infection (STI)] in the past 6 months" (2). The CDC also recommends PrEP for HIV-negative MSM who are in a relationship with an HIV-positive partner. While this recommendation is useful, it omits important factors that may contribute to the risk for HIV infection, such as substance use, frequency of sexual contact, and other predictors shown to be related to HIV infection (3-4).

In a longitudinal analysis of HIV risk and infection among initially HIV-negative MSM, Menza et al. found that initially HIV-negative MSM who eventually tested HIV-positive were more likely at baseline to have a history of STIs, used inhaled nitrates or methamphetamines, engaged in condomless anal intercourse (CAI) with an individual of HIV-positive or unknown status, and to have ten or more partners in the past year, compared to individuals who remained HIV-negative (3). In a subsequent study, Smith et al. found that HIV seroconverters were significantly more likely than non-seroconverters to be younger, have a higher number of sex partners, a higher proportion of HIV-positive partners, greater

number of CAI encounters, and report use of either inhaled nitrates or methamphetamine (4). While current PrEP guidelines consider STI history and CAI in determining PrEP candidacy, other predictors of HIV infection including substance use and number of sex partners are not considered.

Syndemics Theory proposes that psychosocial factors should be considered in a comprehensive HIV risk assessment. Briefly, Syndemics Theory proposes that HIV is not one epidemic but instead is a complex web of overlapping epidemics of sexual risk behavior, substance use, and psychosocial conditions (5). Each of these epidemics promote and reinforce each other to determine individual and population level HIV disease burden. While the previous analyses of longitudinal HIV risk considered sexual risk and substance use, subsequent analyses have supported inclusion of additional psychosocial components (6-8).

Guided by Syndemics Theory, the primary aim of this retrospective study is to use behavioral and HIV testing data from a racially diverse sample of HIV-negative MSM to determine the significant variables at baseline predictive of HIV infection at follow-up and subsequently use these findings to construct an HIV risk score to inform PrEP candidacy among MSM. The secondary aim is to compare the fit of the current model to the current CDC PrEP criteria and to HIV risk models proposed by previous studies.

MATERIALS AND METHODS

Data Collection

The Los Angeles LGBT Center (The Center) is a federally-qualified health center that provides primary health care, HIV specialty care, and HIV/STI testing to over 20,000 unique clients annually.

Data were collected for all MSM who received HIV testing services from January 2009 to June 2014. HIV/STI testing counselors conducted face-to-face behavioral risk assessments that included questions on demographics, STI history, behavior during the last sexual encounter, and substance use.

Following the behavioral risk assessment, blood was obtained for HIV testing using the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (OraSure Technologies, Inc., Bethlehem, PA). Provided the initial antibody test was positive, a second confirmatory Uni-Gold™ Recombigen® HIV-1/2 antibody test (Trinity Biotech, Wicklow, Ireland) was performed to confirm HIV infection. HIV nucleic acid amplification testing (NAAT) was performed from remnant specimens of those individuals whose rapid HIV test was negative or individuals whose first antibody test was positive but second antibody test was either negative or inconclusive. Individuals electing to also receive STI testing were instructed to self-collect urine and rectal samples for *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT). A lab assistant collected a throat swab for pharyngeal NG testing and obtained additional blood to test for *Treponema pallidum* (syphilis) via rapid plasma reagin testing.

Individuals are included in the analysis if they 1) identified as MSM, 2) tested HIV-negative at their baseline visit, 3) reported sex with another man in the year prior to their baseline visit, 4) tested for HIV on at least one occasion after their baseline visit during the analysis period, and 5) had a conclusive HIV result during their final testing visit. MSM are defined as individuals who at their baseline visit reported a biological sex and gender identity of male and, identified either as gay or bisexual or reported having sex with another man in the past year.

Syndemics Theory specifies three constructs (biological, behavioral, and psychosocial) that influence one another and ultimately influence HIV incidence. Each of those domains was represented by questions included within the standard risk assessment. Due to documented differences in HIV incidence by both age group (9) and race/ethnicity (9-11), these demographic covariates are also included in the predictive model.

Statistical Analysis

All predictors used were assessed at baseline. We tested each predictor individually using bivariate Cox proportional hazards models for continuous predictors and bivariate Kaplan-Meier estimators with log-rank tests for categorical predictors. We checked the proportional hazards assumption for predictor variables with the Kolmogorov-type Supremum Test (12), functional form using Martingale residuals, and overall model adequacy (calibration) with the Grønnesby and Borgan test (13). We constructed a multivariable survival model by operationalizing the constructs outlined by Syndemics Theory given the variables available. Neither backward elimination nor forward selection was implemented.

To create the HIV risk algorithm, continuous variables were categorized. Number of sexual partners in the last three months was dichotomized as <=3 and >3 where 3 was the median value. For age difference of the last sexual partner, individuals whose age was within five years of the client age were classified as being of similar age, individuals more than five years older as “Older,” and individuals more than five years younger as “Younger.”

All categorical predictors were then arranged so the reference group was the lowest risk group. We refit the multivariable model with the original categorical predictors and the new categorical predictors for number of sexual partners and age of last sexual partner. Coefficients were added for each individual in the dataset who had values for all predictors. The sum was then exponentiated to create a risk score that compares that person's hazard of HIV infection to the hazard of a hypothetical person in the lowest risk group (14-16). After rounding to the nearest integer, the final range of risk scores was between 1 and 74. The proportion of HIV-positives and HIV-negatives with risk scores greater than or equal to each risk score cut-point were tabulated.

To assess model discrimination, we applied the techniques outlined by Harrell et al. (17) by first sampling 9,481 patients with replacement from the original sample (bootstrap sample). We fit single predictor survival analyses on the bootstrap sample for each of the 18 predictors available that were not deemed to be multi-collinear. Predictors significant at $p = 0.05$ were combined into a bootstrap multivariable survival model (bootstrap full model). The bootstrap full model was fit on the bootstrap sample. Records not included in the

original bootstrap sample formed the holdout sample. The C-statistic was calculated on the holdout sample, and this process was repeated 100 times. The 100 C-statistics were then averaged to measure predictive accuracy of the model (Harrell's C-index).

Lastly, we evaluated the extent to which our model compares with previously published models from Menza et al. (3), Smith et al. (4), and the CDC criteria for PrEP (2). Specifically, we selected variables from our dataset most closely approximating measures described in these publications, and then used these variables to re-fit all of the hazard models in our dataset. Therefore, variables from the original studies were adapted as closely as possible using variables from this dataset and subsequently analyzed using these data.

The same sample from the multivariable model (n = 8,898) was used to test the four models. Some variables used in other models were either not available or could not be exactly replicated with our dataset. Akaike Information Criterion (AIC) and Schwarz Bayesian (Information) Criterion (BIC) were used to compare the models; lower values indicate better fit with the data (18). CDC criteria were compared to our model using an F test. All analyses were performed using SAS Version 9.4 (Cary, NC).

RESULTS

Between January 2009 and June 2014, a total of 9,481 unique MSM tested HIV-negative at baseline and had at least one subsequent HIV testing visit in the analysis period with a conclusive result. There were 370 HIV infections over a period of 16,894 person-years for an HIV positivity rate of 2.18 infections per 100 person-years. The mean amount of follow-up time for all subjects was 651 days (SD = 497 days). The majority of individuals had less than one year of follow-up time (37%), followed by between 1 and 2 years (25%), 2 and 3 years (18%), 3 and 4 years (10%), and more than 4 years (9%). The number of HIV testing visits over the 5.5 years of follow-up did not differ between MSM who were positive and negative at the end of follow-up (Median = 3; Mean = 4).

Bivariate Tests

Hispanic and African-American MSM were more likely to seroconvert over time compared to White individuals (**Table 1**). Younger individuals at baseline were also more likely to seroconvert over time. There were no statistical differences between seroconverters and non-seroconverters by sexual orientation.

Individuals who reported a history of chlamydia, gonorrhea, and/or syphilis were more likely to seroconvert when compared to individuals who reported no reported history of these STIs (**Table 2**). In addition, individuals who tested positive for any of these STIs at baseline were more likely to seroconvert at follow-up.

Seroconverters were more likely than non-seroconverters to report not using condoms during last receptive anal sex and to report more sexual partners in the last 30 days (mean = 3.2 sex partners for HIV-positives vs. 2.5 sex partners for HIV-negatives) and the last three months (6.8 sex partners for HIV-positives vs. 4.9 sex partners for HIV-negatives) (**Table 3**). Seroconverters were also more likely to report their last sex partner was the same race/

ethnicity compared to non-seroconverters and to report an older partner at last sex. For the psychosocial construct, individuals who reported intimate partner violence (IPV) were more likely to seroconvert compared to individuals who did not report IPV.

Seroconverters were more likely to report past year use of ecstasy, methamphetamine, and inhaled nitrates(**Table 4**) compared to non-seroconverters. However, HIV seroconversion was not associated with non-prescription use of erectile dysfunction drugs, cocaine, or alcohol use prior to sex.

Multivariable Results

The multivariable model showed that Hispanic and African-American MSM were more likely to seroconvert compared to White MSM (**Table 5**). MSM who reported a history of chlamydia, gonorrhea, and/or syphilis in the past year were more likely to seroconvert compared to individuals who never reported these infections. MSM who reported receptive anal sex at the last sexual encounter, either with condoms or without, were more likely to seroconvert compared to individuals who did not report this behavior. MSM who reported that their last sex partner was the same race/ethnicity had a higher hazard of seroconversion than MSM who reported a different race/ethnicity. More sexual partners in the last three months also led to a higher hazard of seroconversion. IPV also had a marginally significant association with seroconversion. Lastly, individuals who reported using methamphetamine and/or inhaled nitrates in the past year were more likely to seroconvert. The only variables in the final model not significantly associated with HIV seroconversion were age group, age difference of the last sex sexual partner, and ecstasy use.

Construction of the Risk Score

Following risk score creation, a table was created showing the total number of MSM included, number of HIV-positive MSM, HIV-negative MSM who had scores greater than or equal to each HIV risk score cut-point, and the number of HIV infections per 100 person-years for each risk score (**Table 6**). Approximately 51% of all MSM had a risk score greater than or equal to 5.

If all individuals in our population who had a risk score greater than or equal to five (51%) had been given PrEP, 75% of HIV infections would be averted during follow-up, assuming adequate regimen adherence and near complete effectiveness. In comparison, the CDC criteria would recommend PrEP for 69% of all MSM in this dataset averting 86% of all infections provided positives were instead given PrEP and maintained appropriate adherence. Therefore, the additional variables proposed allow for more targeted PrEP use than current CDC criteria. Physicians, their patients, and other interested individuals can obtain their own personalized risk score by visiting www.IsPrEPforMe.org.

Comparison to Other Models

Harrell's C-index on the 100 hold-out samples was 0.6 showing adequate model predictive accuracy. We also compared our risk score model with CDC criteria and risk score models by Menza et al. and Smith et al. (**Table 7**). Our model had an AIC of 6,094, while the model that generated the CDC criteria had an AIC of 6,162 (2). The BIC for our model (6,160) also

demonstrated a better fit than the CDC model (6,170). The additional predictors included in the present study provide a significantly better fit to the data compared with the original CDC model ($p < 0.0001$).

DISCUSSION

This study found that HIV infection at follow-up was significantly associated with baseline race/ethnicity; self-reported history of chlamydia, gonorrhea, and/or syphilis; condom use during last receptive anal sex; same race/ethnicity of the last sex partner; number of sex partners in the last three months; IPV; methamphetamine use and nitrates use. We created an empirically-based sexual risk score based on study measures. Our calculations indicated that treating 51% of the population with PrEP had the potential to prevent up to 75% of the HIV infections during follow-up at the chosen cut-point of five, provided that participants both initiate PrEP and adhere to the recommended regimen during the entire period that their risk remains significant. A previous mathematical model suggested that treating 50% of a cohort with PrEP would avert 29% of HIV infections over the next 20 years, given medication adherence levels seen in the iPrEx study (19-20).

The better model fit of the current study compared to current CDC criteria shows that predictions of who will seroconvert are more reliable when partner-level variables are considered in addition to STI history and condom use variables. Further, when a client is unsure of their PrEP candidacy, this additional information can improve the guidance given about HIV risk and advisability of PrEP initiation.

Given our findings, we recommend PrEP for MSM with a risk score greater than or equal to five (equivalent in our sample to approximately 2 HIV infections per 100 person-years). If they have a risk score of 8 or higher, we strongly recommend PrEP (equivalent in our sample to approximately 3 infections per 100 person-years). For individuals whose risk score is less than five but who request PrEP, we believe the provider should consider it in light of their patient's overall concerns.

Our study has a number of limitations in both the dataset and analysis. First, although AIC and BIC were compared between the Menza et al. and Smith et al. studies and the CDC criteria, some variables in the previous studies were not identical to those in the current analysis. Further, a serious limitation with the comparison is that our model was developed on our data, while the other models were developed on other datasets, and this provides a bias of unknown size in favor of our model. Second, 6.1% of the population was omitted from the final multivariable model due to missing values one or more variables. Third, recall bias is likely present since certain experiences may be easier to remember than others.

Fourth, there are numerous variables for which we had no data but which probably have a quantifiable relationship with HIV incidence. For example, sexual compulsivity and childhood sexual abuse have recently been shown to have a relationship with HIV acquisition (21-26). In addition, population-level variables in the region where one meets sexual partners, including community viral load and STI prevalence, also impact HIV incidence and should be considered. In addition, certain variables that were measured may

be proxies for other variables that were not available for this analysis. For example, we found that racial/ethnic concordance with the last sex partner was associated with higher HIV risk. This variable may actually be a proxy for breadth of sexual network and more nuanced analyses are needed to explore this relationship.

Lastly, PrEP-specific factors such as willingness to take a daily medication, medication adherence, and concern over side effects should also be considered. Data on these variables were not collected during the analysis period, but future studies should evaluate how these psychosocial, population-level and PrEP-specific predictors can be used to further hone calculations of HIV acquisition risk and subsequently PrEP candidacy.

Lastly, the development of this score was geographically limited to the Los Angeles area. Furthermore, both the current study and the original Menza study used samples collected from the Western Coast of the United States. Validation of these measures are needed in areas where the HIV epidemic is concentrated the most such as cities in the Southern United States.

Despite these limitations, our study has a number of strengths. Previous HIV risk models have had a dearth of racial/ethnic minority subjects which represent the majority of new HIV infections (3-4). In contrast, 52% of our study's sample identified as a racial/ethnic minority. Furthermore, our analyses were informed by a well-tested theory for HIV acquisition in MSM. Syndemics theory, validated in numerous populations of MSM, introduced a psychosocial component which likely impacts HIV incidence and should be explored, especially for racial/ethnic minority MSM. The fit of our model was significantly better relative to CDC guidelines. We have shown that partner-level variables must be considered alongside STI history and substance use variables to build a truly comprehensive risk score. Another strength is that potential PrEP users can use our interactive website to predict their HIV risk and thus PrEP candidacy (www.IsPrEPforMe.org) so that they can be prepared before discussing with their medical provider. Lastly, and most importantly, we have proposed more defined PrEP criteria for MSM when compared to current CDC criteria. While our model does not elucidate every factor that should be considered in determining PrEP initiation, it does represent an improvement over existing CDC guidelines and it points the way for inclusion of ever more relevant variables to permit increasingly more informed decisions about PrEP use.

Our proposed HIV risk algorithm provides a systematic tool for both providers and patients in the biomedical prevention era. Providers will be able to make a more personalized recommendation for each client. Clients will be better informed about what actions and circumstances specifically lead to their increased HIV risk. This, in turn can be empowering and engender a sense of personal agency for each client so they can better decide to initiate PrEP, reduce sexual risk, or make a plan that incorporates both PrEP initiation and sexual risk reduction.

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SHORT SUMMARY

This study proposed to refine CDC pre-exposure prophylaxis criteria for men who have sex with men by creating a personalized HIV Risk Algorithm using HIV testing and behavioral data from a large community-based organization.

Table 1

Bivariate Survival Analyses of Demographics at Baseline by Final HIV Serostatus (n = 9,481), January 2009 - June 2014.

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Orientation				$p = 0.87$
Gay/Homosexual	7,774	319	14,573	2.19
Bisexual	1,105	44	1,963	2.24
Other	232	7	358	1.96
Race/Ethnicity				$p < 0.0001$
White	4,444	146	8,269	1.77
Hispanic	2,841	156	5,428	2.87
Black	708	35	1,237	2.83
Other	1,108	33	1,955	1.69
Missing	10	0	5	0.00
Age Group*				$p = 0.0004$
<25	2,336	118	4,192	2.81
25-29	2,338	105	4,288	2.45
30-39	2,525	97	4,711	2.06
40+	1,912	50	3,702	1.35
Total	9,111	370	16,894	2.18

*The age range was 18-85. The mean age for the HIV-negatives at baseline was 31.7 years old, and the mean age for the HIV-positives at baseline was 29.5 years old. An independent samples t-test using the continuous age variable showed a significant difference between groups by final serostatus ($p < 0.0001$).

Table 2

Bivariate Survival Analyses of Biological Risk Behaviors at Baseline by Final HIV Serostatus (n = 9,481), January 2009 - June 2014.

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Chlamydia Testing Result				$p < 0.0001$
Negative	7,472	279	14,088	1.98
Positive	1,030	77	1,856	4.15
Missing	609	14	949	1.47
Gonorrhea Testing Result				$p < 0.0001$
Negative	7,292	270	13,805	1.96
Positive	1,230	87	2,178	3.99
Missing	589	13	910	1.43
Syphilis Testing Result				$p = 0.0004$
Negative	7,973	303	14,949	2.03
Positive	86	10	158	6.31
Missing	1,052	57	1,787	3.19
Tested Positive for any STI				$p < 0.0001$
Negative	6,052	188	11,523	1.63
Positive	2,100	141	3,753	3.76
Missing	959	41	1,618	2.53
History of Chlamydia				$p < 0.0001$
Never Diagnosed	7,390	265	13,489	1.96
Diagnosed More than One Year Ago	1,310	70	2,553	2.74
Diagnosed within the Last Year	353	33	694	4.76
Missing	58	2	159	1.26
History of Gonorrhea				$p < 0.0001$
Never Diagnosed	6,803	239	12,161	1.97
Diagnosed More than One Year Ago	1,811	81	3,681	2.20
Diagnosed within the Last Year	429	48	866	5.54
Missing	68	2	185	1.08
History of Syphilis				$p = 0.0002$
Never Diagnosed	8,482	326	15,527	2.10
Diagnosed More than One Year Ago	363	21	706	2.98
Diagnosed within the Last Year	172	19	409	4.64
Missing	94	4	251	1.59
History of Herpes Simplex Type II				$p = 0.26$
Never Diagnosed	7,892	333	14,677	2.27
Diagnosed More than One Year Ago	401	10	717	1.39
Diagnosed within the Last Year	144	7	291	2.40
Missing	674	20	1,208	1.65
History of Chlamydia, Gonorrhea and/or Syphilis				$p < 0.0001$

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Never Diagnosed	4,374	116	7,801	1.49
Diagnosed More than One Year Ago	1,975	66	3,952	1.67
Diagnosed within the Last Year*	2,682	187	4,933	3.79
Missing	80	1	208	0.48
Total	9,111	370	16,894	2.18

*Individuals who tested positive at baseline for an STI were classified as “Diagnosed within the Last Year”

Table 3

Bivariate Survival Analyses of Sexual Behavioral and Psychosocial Risks at Baseline by Final HIV Serostatus (n = 9,481), January 2009 - June 2014.

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Had Insertive Anal Sex at Last Sex				$p = 0.02$
No	5,166	190	9,703	1.96
Yes with a Condom	1,884	77	3,617	2.13
Yes without a Condom	1,994	98	3,355	2.92
Missing	67	5	220	2.27
Had Recepitve Anal Sex at Last Sex				$p < 0.0001$
No	5,623	178	10,725	1.66
Yes with a Condom	1,646	75	3,019	2.48
Yes without a Condom	1,818	116	3,093	3.75
Missing	24	1	57	1.75
Had Vaginal Sex at Last Sex				$p = 0.14$
No	8,447	341	15,550	2.19
Yes with a Condom	76	0	112	0.00
Yes without a Condom	250	6	379	1.58
Missing	338	23	853	2.70
Venue for Meeting Sexual Partners				$p = 0.55$
In Person	2,320	96	4,697	2.04
Online	1,537	78	3,295	2.37
More than One	2,243	84	3,269	2.57
Missing	3,011	112	5,633	1.99
Race/Ethnicity of the Last Sex Partner				$p = 0.05$
Same Race/Ethnicity	5,430	243	10,195	2.38
Different Race/Ethnicity	3,471	124	6,343	1.96
Missing	210	3	356	0.84
Age of the Last Sex Partner				$p = 0.05$
More than 5 Years Older	2,182	100	3,966	2.52
Within Five Years of Age	4,652	194	8,468	2.29
More than 5 Years Younger	2,161	71	4,179	1.70
Missing	116	5	281	1.78
Number of Partners in the Past 30 Days				$p < 0.0001$
Mean	2.46	3.17		N/A
Median	2	2		N/A
Standard Deviation	3.3	4.31		N/A
Number of Partners in the Past 3 Months				$p < 0.0001$
Mean	4.92	6.78		N/A
Median	3	4		N/A
Standard Deviation	7.32	10.5		N/A
Intimate Partner Violence (Collapsed)				$p = 0.0004$

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Never	8,268	319	15,195	2.10
Ever, Past Year, or Past Three Months	736	50	1,411	3.54
Missing	107	1	288	0.35
Total	9,111	370	16,894	2.18

Table 4

Bivariate Survival Analyses of Substance Use at Baseline by Final HIV Serostatus (n = 9,481), January 2009 - June 2014.

	HIV-negatives (n = 9,111)	HIV-positives (n = 370)	Person-Years	Number of HIV Infections per 100 Person-Years
Used Ecstasy in the Past 12 Months				$p < 0.0001$
No	8,209	310	15,124	2.05
Yes	828	58	1,576	3.68
Missing	74	2	193	1.03
Used Methamphetamine in the Past 12 Months				$p < 0.0001$
No	8,557	320	15,813	2.02
Yes	476	48	881	5.45
Missing	78	2	199	1.00
Used Inhaled Nitrates in the Past 12 Months				$p < 0.0001$
No	7,680	269	14,138	1.90
Yes	1,352	98	2,560	3.83
Missing	79	3	195	1.53
Used ED Drugs in the Past 12 Months				$p = 0.84$
No	8,394	342	15,416	2.22
Yes	635	26	1,266	2.05
Missing	82	2	212	0.94
Used Cocaine in the Past 12 Months				$p = 0.26$
No	8,030	321	14,894	2.16
Yes	998	47	1,782	2.64
Missing	83	2	219	0.92
Alcohol Use (Before Sex) in the Past 12 Months				$p = 0.81$
No	5,186	199	8,841	2.25
Yes	3,854	170	7,883	2.16
Missing	71	1	170	0.59
Drug Count (Does Not Include Alcohol)				$p < 0.0001$
0	6,328	209	11,671	1.79
1	1,632	82	2,951	2.78
2	784	52	1,470	3.54
3	130	11	236	4.65
4	92	6	190	3.16
5	33	5	76	6.60
Missing	112	5	299	1.67
Total	9,111	370	16,894	2.18

Table 5

Multivariable Survival Analyses of Demographic, Biological, Sexual Behavioral, and Substance Use Measured Constructs at Baseline by Final HIV Serostatus (n = 8,898 / n = 9,481), January 2009 - June 2014.*

	Estimate*	SE	p-value	HR (95% CI)
Race/Ethnicity				$p < 0.0001$
Black	0.68	0.20	0.0009	1.97 (1.32-2.94)
Hispanic	0.52	0.12	<.0001	1.68 (1.32-2.14)
White	Ref	--	--	--
Other	0.27	0.22	0.22	1.31 (0.85-2.00)
Age Group				$p = 0.16$
<25	0.48	0.21	0.02	1.62 (1.07-2.45)
25-29	0.36	0.20	0.07	1.44 (0.97-2.13)
30-39	0.27	0.19	0.15	1.32 (0.91-1.90)
40+	Ref	--	--	--
History of Chlamydia, Gonorrhea and/or Syphilis				$p < 0.0001$
Never Diagnosed	Ref	--	--	--
Diagnosed More than One Year Ago	0.19	0.16	0.23	1.21 (0.89-1.66)
Diagnosed Less than One Year Ago	0.75	0.12	<.0001	2.13 (1.67-2.70)
Receptive Anal Sex at Last Sex				$p < 0.0001$
No	Ref	--	--	--
Yes With Condom	0.35	0.14	0.01	1.42 (1.08-1.87)
Yes Without Condom	0.61	0.12	<.0001	1.84 (1.45-2.35)
Race/Ethnicity of Last Sex Partner				
Different Race/Ethnicity	Ref	--	--	--
Same Race/Ethnicity	0.45	0.13	0.0004	1.57 (1.23-2.02)
Age of Last Sex Partner	0.005	0.01	0.51	1.01 (0.99-1.02)
Number of Sexual Partners in the Last 3 Months	0.01	0.00	0.003	1.01 (1.00-1.02)
Intimate Partner Violence				
Never	Ref	--	--	--
Ever, Past Year, or Past Three Months	0.31	0.16	0.05	1.36 (1.00-1.85)
Used Ecstasy in the Past 12 Months				
No	Ref	--	--	--
Yes	0.21	0.16	0.19	1.23 (0.90-1.67)
Used Methamphetamine in the Past 12 Months				
No	Ref	--	--	--
Yes	0.49	0.17	0.005	1.64 (1.17-2.30)
Used Inhaled Nitrates in the Past 12 Months				
No	Ref	--	--	--
Yes	0.45	0.13	0.0006	1.57 (1.21-2.03)

*The estimates were added for each individual and then exponentiated to obtain each risk score. Number of sex partners in the last three months was dichotomized at the median of 3 (Less than or equal to 3 versus More than 3). Age of Last Sex Partner was divided into three categories: 1) More than 5 Years Older; 2) Within Five Years of Age; 3) More than 5 Years Younger.

Table 6

Sensitivity and Specificity for HIV Risk Algorithm Cut-Points (Range: 1-74) (n = 8,898)

All MSM			HIV Positives			HIV Negatives		
Cut Point	% greater than or equal to Cut-Point	n	Number of HIV Infections per 100 Person-Years	Number greater than or equal to Cut-Point*	Sensitivity % greater than or equal to Cut-Point	n	Number greater than or equal to Cut-Point*	1-Specificity % greater than or equal to Cut-Point
1	100.0%	0	0.00	362	100.0%	158	8,536	100.0%
2	98.2%	13	0.53	362	100.0%	1306	8,378	98.1%
3	83.4%	32	1.11	349	96.4%	1581	7,072	82.8%
4	65.3%	47	2.04	317	87.6%	1240	5,491	64.3%
5	50.8%	36	1.94	270	74.6%	1010	4,251	49.8%
6	39.1%	22	1.75	234	64.6%	701	3,241	38.0%
7	30.9%	18	1.97	212	58.6%	523	2,540	29.8%
8	24.8%	29	3.25	194	53.6%	466	2,017	23.6%
9	19.3%	22	3.98	165	45.6%	323	1,551	18.2%
10	15.4%	19	4.28	143	39.5%	235	1,228	14.4%
11	12.6%	14	4.61	124	34.3%	167	993	11.6%
12	10.5%	22	9.52	110	30.4%	145	826	9.7%
13	8.6%	14	7.23	88	24.3%	107	681	8.0%
14	7.3%	10	5.03	74	20.4%	88	574	6.7%
15	6.2%	9	6.80	64	17.7%	76	486	5.7%
16	5.2%	7	5.68	55	15.2%	70	410	4.8%
17	4.4%	5	4.33	48	13.3%	63	340	4.0%
18	3.6%	7	7.41	43	11.9%	49	277	3.2%
19	3.0%	7	11.79	36	9.9%	35	228	2.7%
20	2.5%	3	5.25	29	8.0%	26	193	2.3%
21	2.2%	4	5.44	26	7.2%	37	167	2.0%
22	1.7%	1	5.02	22	6.1%	11	130	1.5%
23	1.6%	5	13.42	21	5.8%	20	119	1.4%
24	1.3%	2	11.53	16	4.4%	10	99	1.2%
25	1.2%	0	0.00	14	3.9%	8	89	1.0%
26	1.1%	3	24.14	14	3.9%	7	81	0.9%
27	1.0%	2	15.66	11	3.0%	9	74	0.9%
28	0.8%	1	9.92	9	2.5%	6	65	0.8%
29	0.8%	0	0.00	8	2.2%	8	59	0.7%
30	0.7%	1	11.24	8	2.2%	5	51	0.6%
31	0.6%	0	0.00	7	1.9%	4	46	0.5%
32	0.6%	0	0.00	7	1.9%	6	42	0.5%
33	0.5%	1	51.28	7	1.9%	2	36	0.4%
34	0.4%	0	0.00	6	1.7%	7	34	0.4%
35	0.4%	1	55.87	6	1.7%	2	27	0.3%
36	0.3%	0	0.00	5	1.4%	1	25	0.3%

All MSM			HIV Positives			HIV Negatives		
Cut Point	**% greater than or equal to Cut-Point**	**n**	**Number of HIV Infections per 100 Person-Years**	**Number greater than or equal to Cut-Point***	**Sensitivity % greater than or equal to Cut-Point**	**n**	**Number greater than or equal to Cut-Point***	**1-Specificity % greater than or equal to Cut-Point**
37	0.3%	1	13.30	5	1.4%	5	24	0.3%
38	0.3%	0	0.00	4	1.1%	2	19	0.2%
39	0.2%	0	0.00	4	1.1%	0	17	0.2%
40 or above	0.2%	4	11.11	4	1.1%	17	17	0.2%
Total		362				8,536		

*Calculated by subtracting the cumulative sum before that row from the total for each category

Table 7

Comparison of the Akaike Information Criterion between Studies (n = 8,846)

Study	Variables Reported in Original Study	Equivalent Variables Used in this Dataset to Calculate Akaike Information Criterion	Akaike Information Criterion	Schwarz Bayesian Criterion
CDC 2014	Any anal sex without condoms (receptive or insertive) in past 6 months Any STI diagnosed or reported in past 6 months Is in an ongoing sexual relationship with an HIV-positive male partner	Any anal sex without condoms (receptive or insertive) at the last sexual experience Any STI reported in past 12 months	6,162	6,170
Smith 2012	Age Number of Sex Partners, prior 6 months Number of receptive anal sex episodes, prior 6 months Number of sex partners who were HIV positive Number of insertive anal sex episodes with an HIV+ man, prior 6 months Methamphetamine use, prior 6 months Nitrates use, prior 6 months	Age Number of Sex Partners, Last 3 Months Condom Use during receptive anal sex, last partner Condom Use during insertive anal sex, last partner Methamphetamine use, prior 12 months Nitrates use, prior 12 months	6,150	6,188
Menza 2009	Race/Ethnicity Age Diagnosis or History of an STI at Baseline Methamphetamine or Nitrates use, prior 6 months >= 10 Male Sex Partners, Prior Year Receptive, non-concordant unprotected anal sex, prior year	Race/Ethnicity Age History of any STI Methamphetamine or Nitrates Use, prior 12 months Number of Sex Partners, Last 3 Months Condom Use during receptive anal sex, last partner	6,073	6,115
LALGT Center Data	Race/Ethnicity Age History of any STI Condom Use during receptive anal sex, last partner Race/Ethnicity, last partner Age Difference, last partner Number of Sex Partners, Last 3 Months Intimate Partner Violence Ecstasy use, prior 12 months Methamphetamine use, prior 12 months Nitrates use, prior 12 months	N/A	6,094	6,160