Alcohol, Tobacco, and Illicit Drug Use as Risk Factors for Onward HIV Transmission Among Men Who Have Sex with Men & Transgender Women in Lima, Peru

Katherine Vanessa Garcia-Rosales

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2018

Committee:

Ann C. Duerr

Stephen E. Hawes

Joshua T. Herbeck

Angela K. Ulrich

Program Authorized to Offer Degree:

Epidemiology

University of Washington

Abstract

Alcohol, Tobacco, and Illicit Drug Use as Risk Factors for Onward HIV Transmission Among Men Who Have Sex with Men & Transgender Women in Lima, Peru

Katherine Vanessa Garcia-Rosales

Chair of the Supervisory Committee:

Ann C. Duerr

Department of Global Health

In 2016, there were about 70,000 (55,00–94,000) people living with HIV in Peru, with a prevalence of 16.4% among men who have sex with men (MSM) and 18.5% among transgender people.[1] The aim of this study was to assess the association of heavy drinking, AUDIT score, tobacco use, and illicit drug use as independent risk factors for onward HIV transmission among MSM and transgender women in Lima, Peru. We identified 201 participants with incident HIV and used multivariate logistic regression to compare the association of each risk factor with onward HIV transmission (cluster membership assessed by phylogenetic analysis). Participants who reported heavy drinking (aOR: 1.51; 95% CI: 0.70-3.28) or had an AUDIT score ≥20 (aOR: 1.30; 95% CI: 0.47-3.65) had similar but not significantly higher odds of clustering. Current smoking status (aOR: 0.41; 95% CI: 0.10-1.73) or illicit drug use (aOR: 0.53; 95% CI: 0.19-1.49) were not associated with cluster membership. Our study findings suggest that there is a great need to focus on identifying other potential risk factors for onward HIV transmission.

Introduction

In Peru, the majority of new HIV cases continue to occur among men who have sex with men (MSM), sex workers, transgender people, and people in prison.[1] The prevalence of HIV among MSM is 13 times higher than in the general population of Peru and about 70% of all Peruvians infected with HIV reside in Lima.[2,3] Drug use and alcohol abuse are associated with increased risk of both acquiring and transmitting HIV among MSM and transgender women (TW).[4] In Peru, there is data indicating that illicit drug use is associated with twice the likelihood of engaging in sex with a casual partner in the past year, a 50% reduction in condom use, and three times the risk of symptomatic STIs.[3,5] Nonetheless, the association of licit or illicit drug use and HIV transmission (as opposed to HIV acquisition or prevalent HIV infection) has not been widely investigated among MSM and TW in Peru.

Use of Phylogenetics.

Phylogenetics can be used as an epidemiological tool to characterize transmission networks in a population because HIV isolates from donor-recipient and transmission pairs are more genetically similar to each other than to other viruses.[6] Phylogenetic clusters can be particularly informative about transmission patterns, as studies have found that individuals with clinical, behavioral, or demographic factors linked with higher relative rates of transmission are often over-represented in clusters.[7] Clusters are commonly identified through the use of specific inclusion thresholds based on genetic distance or phylogenetic branch length.

Alcohol

The most commonly used drug in Peru is alcohol with an estimated lifetime prevalence of 83% (in 2006), and alcohol use disorder (AUD) is reported five times higher among MSM and TW compared to the general male population (63% vs. 12%).[3,8,9] In a Peruvian population, heavy

episodic drinking was associated with risky sexual behaviors that included false sex expectations, having multiple sexual partners or a casual partner in the past year, and not using condoms.[3,5] Although many studies have demonstrated a link between alcohol use and HIV risk behavior or HIV acquisition, there have been fewer studies investigating the link between alcohol consumption among HIV-infected persons and onward HIV transmission.

Smoking Tobacco

Recent studies suggest that the prevalence of cigarette smoking among people living with HIV is twice the prevalence when compared to the general population.[10–12] The risk profile for acquiring HIV includes characteristics similar to those populations that have a higher likelihood of using tobacco. These characteristics include low socioeconomic status, history of illicit substance use or abuse, and identifying as gay or bisexual.[13] While tobacco use is common among HIV-infected populations, this is likely due to its overlap with other lifestyle factors (i.e. alcohol use) that are associated with increased risk of HIV acquisition rather than a direct impact on risk of acquiring or transmitting HIV. Research suggests that the higher rates of smoking among MSM may be associated with other cultural and gender-based social situations.[10,14] Due to a history of exclusion and discrimination in many social settings, the social focus for MSM has been gay bars and clubs where the prevalence of smoking is high.[10,14] However, there is very little research on the effect of smoking on acquisition or transmission of HIV, and the few studies that focused on this relationship found little evidence that smoking increased the risk for HIV acquisition.

Illicit Drug Use

In a study that examined sexual behavior and drug consumption, drug use was associated with high-risk sexual behaviors even after controlling for alcohol consumption.[5] It is known that

recreational substance use and substance use disorders are risk factors for acquiring HIV.[14] There is increasing evidence that use of club drugs (i.e. methamphetamine (most common club drug)) is associated with increasing prevalence of HIV among MSM by increased risk for engaging in HIV risk-related sexual behaviors.[14,15] In examining the association between HIV-positivity, risky behaviors, and drug use in Peru, several studies have found that people who reported using cocaine before or during sex were at increased risk of being HIV-positive.[3,16] One study found that MSM who reported using cocaine and having sex with men in the past year had double the risk of being HIV-infected compared to non-cocaine users.[3,16]

Currently, there is evidence that supports the relationship between alcohol, illicit drugs, and HIV transmission, but more research is needed in investigating the risk of onward transmission. The goal of this study is to investigate if alcohol, tobacco, or illicit drug use are risk factors for onward HIV transmission (risk of transmitting HIV as opposed to risk of acquiring HIV) among men who have sex with men and transgender women in Lima, Peru. We used phylogenetic cluster analysis as an indicator of higher rates of onward HIV transmission among MSM and TW populations in Lima. We assessed heavy drinking, alcohol use disorders identification test (AUDIT) scores, current use of cigarettes, and any reported illicit drug use as risk factors. We hypothesize that heavy drinking, AUDIT score $\geq$20, and any illicit drug use will be independently associated with onward HIV transmission. Additionally, we hypothesize that current cigarette smoking will not be independently associated with onward HIV transmission.

Methods

Study Design, Data sources, Population:

The *Sabes* study; *HIV Testing and Treatment to Prevent HIV Transmission Among MSM and Transgender Women (Sabes*? meaning "Do you know?"), collected data from MSM and TW

in Lima, Peru from 2013 to 2017.[17] *Sabes* was comprised of three steps: Step 1) HIV screening of 3,337 high-risk participants; Step 2) follow-up of 2,109 HIV-uninfected participants for 24 months with monthly testing; and Step 3) enrollment of participants who tested HIV-positive (enrolled 216 of 254 HIV-positive) into a antiretroviral treatment initiation study.[17] The parent study sequenced ~700 nucleotides of the *pol* (partial reverse-transcriptase and partial protease) gene from 311 participants. The *pol* sequences are used to infer transmission dynamics and are linked to epidemiological data to identify potential risk factors for onward HIV transmission. The current study is an exploratory cross-sectional analysis of 201 incident HIV cases identified during follow-up in the *Sabes* study for whom we have behavioral and HIV sequence data.

Institutional Review Board:

For this data analysis, there was no direct contact with any of our study participants as all the data and specimens were already collected by the start of this project. Hence, this study was classified as not human subject research by the University of Washington's IRB.

Outcome of interest:

Onward HIV transmission was assessed through phylogenetic clustering analysis for all 201 incident HIV cases. Evidence of onward HIV transmission (operationally defined as clustering or not clustering in the phylogenetic tree) was delineated using a patristic-distance clustering analysis. Patristic distance is defined by the sum of branch lengths on the path from one tip of the phylogenetic tree to another tip in the tree.[18] This type of phylogenetic analysis is very similar to clustering by pairwise genetic distance and clusters can be constructed from pairs of sequences whose patristic distance is below a cut-off value.[18] Phylogenetic clusters with varying conservative and liberal patristic distance thresholds (0.01, 0.02, 0.045, 0.06) and

different minimum cluster sizes (clusters containing ≥2 or ≥3 *Sabes* cohort members) were identified.

Exposures:

At monthly visits, participants completed a survey regarding their alcohol and illicit drug consumption patterns in the past 30 days. Data from the visit when the participant was diagnosed with HIV was used for this analysis. Other risk factors considered in this analysis included an AUDIT score ≥20 from the *Sabes* baseline enrollment visit and smoking status after HIV diagnosis (Figure 1).

Figure 1: Information on when risk factor was collected

Variable	**Time of Collection**
Binge drinking	Last step 2 visit of *Sabes* study (visit when participant was diagnosed with HIV).
PEth concentration levels	Visit immediately following HIV diagnosis.
AUDIT score	*Sabes* enrollment visit.
Illicit drug use	Last step 2 visit of *Sabes* study (visit when participant was diagnosed with HIV).
Tobacco use	Multiple time points after HIV diagnosis.

Heavy drinking was defined as binge drinking (consuming five or more drinks) on at least one occasion in the 30 days before diagnosis and/or having a blood phosphatidylethanol (PEth) concentration of ≥8 ng/mL. The *Sabes* study collected dried blood spots from participants at the first visit after HIV diagnosis to measure alcohol consumption through the biomarker PEth in red blood cells. This sensitive marker is formed in red blood cells when the body metabolizes ethanol and is a direct marker of chronic alcohol use and abuse.[19,20] There is currently no international PEth concentration cut-off, but there is a national standard in Sweden with a routine clinical threshold of 0.7 uM and a lower limit quantitation of 8 ng/mL (2-3 uM) that has been

used in several studies.[20,21] This study uses the commonly used threshold concentration ≥8 ng/mL as a positive PEth test result. AUDIT score was calculated based on a 10-item questionnaire covering three domains: hazardous alcohol use, dependence symptoms, and harmful alcohol use.[22] The scores for each question ranged from 0-4 with a maximum possible score of 40.[19,22] An AUDIT score between the range of 8-15 represents a medium level of alcohol problem, scores 16-19 references harmful and hazardous drinking behaviors, and a score ≥20 suggests alcohol dependence.[22]

Past-month use of any illicit drug use was assessed with the question, "In the past 30 days, how many days did you use any of the following types of drugs? Do not include drugs used under a doctor's prescription." We collapsed use of illicit drug use to include any use of marijuana, (smoked or inhaled), cocaine, and inhaled poppers (no participants reported using injecting ketamine or other injectable drugs, taking amphetamines orally, or used ecstasy) in the past 30 days.

Smoking status was defined as either a never smoker (person who has smoked <100 cigarettes in their lifetime); current smoker (person who has smoked ≥100 cigarettes in their lifetime and currently smokes); or former smoker (person who has smoked ≥100 cigarettes in their lifetime, but had quit smoking at the time of the interview).[23]

Potential Confounders:

Demographic measures for each participant were abstracted from the baseline survey administered at the enrollment visit in the parent study. Expert opinion and previous literature on this topic was used to empirically identify potential confounders. The potential confounders that

we assessed using data collect at baseline included sexual and gender identity, age, educational level, monthly income, and sex worker status of the participant.

Statistical Analyses

We present descriptive measurements of 201 HIV-positive individuals that include demographic characteristics and information on exposures of interest (e.g. heavy drinking, AUDIT score ≥20, tobacco use, and any illicit drug use). We used logistic regression to build models that evaluate the relationship for each risk factor (one model for each of the four risk factors) with onward HIV transmission (cluster membership). All potential *a priori* confounders were assessed by a change-in-estimate criterion of ≥10% of the effect of exposure within each model. Confounders were included in the final adjusted models when the criteria were met. All the analyses were conducted using STATA/IC 15.1 statistical software. Additionally, we tested robustness of associations with varying cluster thresholds (0.01, 0.02, 0.045, 0.06) and varying minimum cluster sizes (clusters containing ≥2 or ≥3 *Sabes* cohort members).

Results

Among the 201 participants, 55% reported to be 24 years or younger, about ¾ of the participants had complete or partial post-secondary education, 85% had a monthly income <$400, almost 90% identified as MSM, and 10% considered themselves as sex workers. Additionally, 22% reported heavy drinking in the past 30 days, 10% scored an AUDIT ≥20 (dependency), 6% reported being current smokers, and 9% reported having used any illicit drugs in the past 30 days. (Table 1).

For this study, based on common practice found in the literature[18,24] and expert opinion, the models testing each of the four exposures of interest were analyzed using a patristic distance of 0.02 and minimum cluster size of ≥2 *Sabes* participants (cluster analysis 2) with 179 (50%) participants included in clusters with close genetic relatedness. As a sensitivity analysis, we compared eight different cluster analyses with varying patristic distance thresholds and different minimum cluster sizes (clusters containing ≥2 or ≥3 *Sabes* cohort members) (Table 2). Among all eight analyses, clusters analyses 4 and 8 (threshold=0.06) and 7 (threshold=0.045) identified majority of the sample participants in a cluster, and cluster analysis 5 (threshold=0.01) has a very limited number of participants in clusters (Table 3). For the remainder cluster analyses we looked into their frequencies and odds of clustering for the analysis of each risk factor variable (Tables 4a and 4b). The results in the sensitivity analysis supported the patristic-distance threshold and cluster size used in the final models.

In the risk factor logistic models after adjusting for the necessary (age, gender and sexuality, or education level) confounders, participants who reported heavy drinking in the past 30 days (aOR: 1.51; 95% CI: 0.70-3.28) or had an AUDIT score ≥20 (aOR: 1.30; 95% CI: 0.47-3.65) had non-significantly higher odds of clustering. Self-reported current smoking (aOR: 0.41; 95% CI: 0.10-1.73) and illicit drug use in the past 30 days (aOR: 0.53; 95% CI: 0.19-1.49) were non-significantly inversely associated with cluster membership (risk of onward HIV transmission) (Table 5).

Discussion

This study of HIV incident cases characterizes the association between substance use behaviors (alcohol, tobacco, or illicit drug use) as risk factors for onward HIV transmission (cluster membership) among MSM and TW. We found that neither heavy drinking, AUDIT ≥20

score, nor illicit drug use were independently or significantly associated with onward HIV transmission. Additionally, individuals who identified as transgender women were inversely (OR= 0.29; 95% CI: 0.11-0.74) associated with belonging in a cluster; this may be due to the sampling of the parent study. *Sabes* only captured MSM/TW who reported having has sex with a male partner in last 12 months and having a high risk for acquiring HIV (i.e. having unprotected anal intercourse or being a sexual partner of an HIV-infected man or TW in the last 6 months).[17] Partners of these transgender women may identify as heterosexuals and may have been less likely to be enrolled in the parent study. This would result in lower coverage of the sexual networks of these transgender women and we may not have accurately capture their likelihood of onward HIV transmission.

This is the first study to examine the association of use of four licit or illicit substances as risk factors for onward HIV transmission among MSM and TW. Alcohol is the most commonly abused drug in Peru, followed by marijuana with a lifetime prevalence of 3.6%, and cocaine use (smoked and inhaled) with a lifetime prevalence of 2.8%.[3] In a 2013 surveillance report, the Peruvian Ministry of Health found that having anal sex without a condom and having consumed alcohol were independently associated with a recent HIV diagnosis.[25] In Peru, 13.3% of the adult males are current smokers and smoking is particularly a common practice among MSM and TW due cultural and gender-based social situations / clubs.[10,14,26] In these venues, there are certain social and cultural codes of conduct that may reinforce cigarette smoking and are also tied with behaviors that promote high-risk behaviors such as alcohol use, illicit drug use, and unprotected sex.[14] Concurrent use of tobacco with other substances (i.e. alcohol, marijuana, psilocybin, cocaine, LSD, or MDMA) is not uncommon.[14] Irrespective of the non-significant results in this

study, it still provides an exploratory outlook on the risk of onward transmission among MSM and TW who use licit and/or illicit drugs.

This study has a number of limitations. For some of the risk factors, there was potential for recall bias from the participants when asked to recollect their behaviors in the past 30 days with the potential of non-differential misclassification bias of exposure. There is the possibility that the participant may not have remembered all of the details of an experience (i.e. the exact number of drinks they consumed a day) or unintentionally created new memories. However, we expect this bias to be non-differential between those who will have cluster membership vs. no cluster membership. For the heavy drinking risk factor, PEth concentration may vary depending on when the participant consumed alcohol and when they were tested for the PEth phospholipid.[19] The amount of alcohol consumed determines the duration of a positive blood PEth test. For most people the average half-life of PEth is 4.5 days (range of 1-10 days).[19] Due to this decay, participants who stop drinking after HIV diagnosis may test negative at their first post-diagnosis visit which occurred a median of 6 days later. However, we expect this potential bias to be non-differential. Additionally, we have self-reported data on binge drinking collected immediately before the participant was diagnosed with HIV, preventing potential measurement bias relating to knowledge of HIV status.

In regards to identifying clusters, we estimate that our genome sampling density was robust enough to provide an appropriate population coverage. Similar studies examining cluster membership have comparable proportions of MSM who cluster with similar patristic distance threshold as this study.[18,24]

Moreover, there is temporality issue with the tobacco consumption status because data was collected after participants were diagnosed with HIV. However, we estimate that this does

not affect the outcome of clustering because “never smokers” and “ever smokers” categories are expected to change little between the time of HIV diagnosis and collection of data on smoking status. A bigger limitation of this study is the small sample size and missing data for several variables that led to a lack of power to identify an association. Among the total sample size of 201, 37% (n=74) had missing alcohol consumption data and 67% (n=130) had missing tobacco data. The low power reduces the chance of detecting a true effect of association between risk factors and the outcome of clustering.

Regardless of the various limitations in this study, this project is important in the field of HIV and substance use as there is a lack of research on the association between substance use and risk of onward HIV transmission among MSM and TW. While the risk of onward HIV transmission is known to be increased due to needle sharing in general, the impact of non-injection drug use on onward transmission is less clear.[3] Similar studies with bigger sample sizes are needed to further explore this relationship with onward HIV transmission.

Reference:

1. UNAIDS. UNAIDS Data 2017. http://www.unaids.org/sites/default/files/media_asset/20170720_Data_book_2017_en.pdf. Published 2017. Accessed December 4, 2017.
2. De Habich Rospigliosi M, Carlos Del Carmen Sara J, Rebaza H, et al. Informe Nacional Sobre Los Progresos Realizadas en el Pais Peru. 2013. http://www.unaids.org/sites/default/files/country/documents//PER_narrative_report_2014.pdf. Accessed September 30, 2017.
3. Massa A, Rosen M. The Relationship between Substance Use and HIV Transmission in Peru. 2012;31(9):1713-1723. doi:10.1109/TMI.2012.2196707.Separate.
4. Centers for Disease Control and Prevention. HIV and Substance Use in the United States. https://www.cdc.gov/hiv/risk/substanceuse.html. Accessed May 30, 2018.
5. Gálvez-Buccollini JA, DeLea S, Herrera PM, Gilman RH, Paz-Soldan V. Sexual behavior and drug consumption among young adults in a shantytown in Lima, Peru. *BMC Public Health*. 2009;9:1-10. doi:10.1186/1471-2458-9-23.
6. Brenner B, Wainberg MA, Roger M. Phylogenetic inferences on HIV-1 transmission. *Aids*. 2013;27(7):1045-1057. doi:10.1097/QAD.0b013e32835cffd9.
7. Le Vu S, Ratmann O, Delpech V, et al. Comparison of cluster-based and source-attribution methods for estimating transmission risk using large HIV sequence databases. *Epidemics*. 2017;(October):1-10. doi:10.1016/j.epidem.2017.10.001.
8. Ludford KT, Vagenas P, Lama JR, et al. Screening for Drug and Alcohol Use Disorders and Their Association with HIV-Related Sexual Risk Behaviors among Men Who Have Sex with Men in Peru. Grinsztejn BGJ, ed. *PLoS One*. 2013;8(8):e69966.

doi:10.1371/journal.pone.0069966.

9. WHO. Global status report on alcohol and health 2014. *Ctry Profiles, Peru*. 2014.

10. Akhtar-Khaleel W, Cook R, Shoptaw S, et al. Trends and Predictors of Cigarette Smoking Among HIV Seropositive and Seronegative Men: The Multicenter AIDS Cohort Study. *AIDS Behav*. 2013;73(6):622-632. doi:10.1038/pr.2013.52.

11. Vidrine DJ, Frank SG, Savin MJ, et al. HIV Care Initiation: A Teachable Moment for Smoking Cessation? *Nicotine Tob Res*. September 2017. doi:10.1093/ntr/ntx218.

12. Marshall M, McCormack M, Kirk G. Effect of Cigarette Smoking on HIV Acquisition, Progression, and Mortality. *AIDS Educ Prev*. 2009;21(3):81-93. doi:10.1521/aeap.2009.21.3.

13. Burkhalter JE, Springer CM, Chhabra R, Ostroff JS, Rapkin BD. Tobacco use and readiness to quit smoking in low-income HIV-infected persons. *Nicotine Tob Res*. 2005;7(4):511-522. doi:10.1080/14622200500186064.

14. Reynolds NR. Cigarette smoking and HIV: more evidence for action. *AIDS Educ Prev*. 2009;21(3 Suppl):106-121. doi:10.1521/aeap.2009.21.3_supp.106.

15. Kipke MD, Weiss G, Ramirez M, et al. Club drug use in los angeles among young men who have sex with men. *Subst Use Misuse*. 2007;42(11):1723-1743. doi:10.1080/10826080701212261.

16. Lama JR, Lucchetti A, Suarez L, et al. Association of Herpes Simplex Virus Type 2 Infection and Syphilis with Human Immunodeficiency Virus Infection among Men Who Have Sex with Men in Peru. *J Infect Dis*. 2006;194(10):1459-1466. doi:10.1086/508548.

17. Lama JR, Brezak A, Dobbins JG, et al. Design Strategy of the Sabes Study: Diagnosis and Treatment of Early HIV Infection Among Men Who Have Sex With Men and

Transgender Women in Lima, Peru, 2013–2017. *Am J Epidemiol*. March 2018. doi:10.1093/aje/kwy030.

18. Poon AFY. Impacts and shortcomings of genetic clustering methods for infectious disease outbreaks. *Virus Evol*. 2016;2(2):1-9. doi:10.1093/ve/vew031.
19. United States Drug Testing Laboratories. How Much Have They Been Drinking? 2018;9(1):1-16.
20. Viel G, Boscolo-berto R, Cecchetto G, Fais P, Nalesso A, Ferrara S. Phosphatidylethanol in Blood as a Marker of Chronic Alcohol Use : A Systematic Review and Meta-Analysis. *Int J Mol Sci*. 2012;(3):14788-14812. doi:10.3390/ijms131114788.
21. Piano MR, Tiwari S, Nevoral L, Phillips SA. Phosphatidylethanol Levels Are Elevated and Correlate Strongly with AUDIT Scores in Young Adult Binge Drinkers. *Alcohol Alcohol*. 2018;50(May):519-525. doi:10.1093/alcalc/agv049.
22. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Care. 2001. http://www.talkingalcohol.com/files/pdfs/WHO_audit.pdf. Accessed December 8, 2017.
23. National Health Interview Survey. Glossary: Adult Tobacco Use. https://www.cdc.gov/nchs/nhis/tobacco/tobacco_glossary.htm. Published 2017. Accessed February 28, 2018.
24. Poon AFY, Joy JB, Woods CK, et al. The Impact of Clinical, Demographic and Risk Factors on Rates of HIV Transmission: A Population-based Phylogenetic Analysis in British Columbia, Canada. *J Infect Dis*. 2015;211(6):926-935. doi:10.1093/infdis/jiu560.
25. De Habich Rospigliosi M, Carlos Del Carmen Sara J, Rebaza H. *Informe Nacional Sobre Los Progresos Realizados En El País Peru*.; 2013.

26. The Tobacco Atlas. Peru. 2016.

27. The Tobacco Atlas. Country Fact Sheet: Peru. http://www.tobaccoatlas.org/country-data/peru/. Published 2013.

Table 1. Characteristics of newly diagnosed HIV-positive Men who have sex with me and Transgender women - Lima, Peru, 2013-2015

	HIV-positive	
Characteristics	**N**	**%**
Total Participants	201	100
Age		
18-24	111	55
25-34	75	37
≥35	15	8
Education		
No secondary	7	4
Complete or partial secondary	49	24
Complete or partial post-secondary	145	72
Monthly Income		
No income	36	18
<$400	134	67
$400-$799	28	14
≥$800	3	1
Sexuality and Gender Identity		
MSM	178	89
TW	23	11
Sex Work Status		
Yes	21	10
No	179	89
No response/Missing	1	1
Tobacco Use≠		
Never smoker	52	73
Current smoker	11	16
Former smoker	8	11
Alcohol Consumption±		
Heavy drinker	44	35
Not a heavy drinker	83	65
AUDIT Score▽		
≤15	140	75
16-19	26	14
≥20	20	11
Illicit Drug Use (in the past 30 days)		
Any illicit drug useΩ	17	9
Used marijuana	15	7
Did not used marijuana	186	93
Used poppers	6	3
Did not used poppers	195	97
Used cocaine	4	2
Did not used cocaine	197	98

NOTES:

MSM: Men who have sex with men

TW: Transgender women

≠ 130 participant were missing/no response.

± Data collected in parent study in last Step 2 visit before diagnosis. 74 participants had missing/no response. Combined variable if a participant reported binge drinking (≥5 drinks) on at least 1 day in the past 30 days and/or had tested positive (≥8 ng/ml) phosphatidylethanol (PEth) concentration in blood test.

∇ Data collected during parent study enrollment visit with high participation rate; 14 participants reported never drinking alcohol in the past 12 months and 1 had missing data.
Ω Combined variable that includes use of marijuana, (smoked or inhaled) cocaine, injected ketamine or other injectable drugs, drank amphetamines, inhaled poppers, used ecstasy, or any other drug not including alcohol in the past 30 days in the participant's Step 2 last visit.

Table 2. Phylogenetic cluster analysis with different patristic distance thresholds and minimum cluster size cutoffs

Clusters Analysis	Patristic Distance Threshold	Minimum Cluster Size*	Number of Clusters	% *Sabes* Cohort in Clusters^
Analysis 1	0.01	2	95	27%
Analysis 2	0.02	2	179	50%
Analysis 3	0.045	2	282	79%
Analysis 4	0.06	2	315	89%
Analysis 5	0.01	3	43	12%
Analysis 6	0.02	3	129	36%
Analysis 7	0.045	3	265	75%
Analysis 8	0.06	3	313	88%

NOTES:

*Minimum number of *Sabes* participants in cluster analysis

^This percentage was calculated out of n=311, the participants in whom genome sequences were determined.

Table 3. Odds Ratio Associated with risk factor with varying cluster thresholds

Cluster Analysis	Number of participant in clusters n (%)	Risk factor	Number of participants in clusters	Odds Ratio of Clustering*	P-value	95% (CI)
Analysis 1	62 (31)	Heavy Drinker	14 (58)	1.02	0.96	(0.47-2.24)
		Current Smoker^	3 (14)	0.93	0.92	(0.22-3.97)
		Any Illicit Drug Use	4 (6)	0.67	0.50	(0.21-2.14)
		AUDIT score $\geq 20^{\Pi}$	4 (8)	0.60	0.38	(0.19-1.88)
Analysis 2	114 (57)	Heavy Drinker	27 (61)	1.34	0.44	(0.64-2.82)
		Tobacco Use	5 (13)	0.71	0.61	(0.19-2.64)
		Any Illicit Drug Use	7 (6)	0.50	0.18	(0.18-1.38)
		AUDIT score $\geq 20^{\Pi}$	11 (11)	0.98	0.97	(0.39-2.50)
Analysis 3	83 (41)	Heavy Drinker	21 (64)	1.25	0.55	(0.60-2.61)
		Current Smoker^	3 (11)	0.60	0.49	(0.14-2.53)
		Any Illicit Drug Use	6 (6)	0.57	0.30	(0.19-1.67)
		AUDIT score $\geq 20^{\Pi}$	8 (11)	0.96	0.93	(0.37-2.48)
Analysis 4	200 (99)	Heavy Drinker	44 (59)	1.00	-	-
		Current Smoker^	11 (15)	1.00	-	-
		Any Illicit Drug Use	17 (9)	1.00	-	-
		AUDIT score $\geq 20^{\Pi}$	20 (11)	1.00	-	-
Analysis 5	34 (17)	Heavy Drinker	8 (67)	1.31	0.58	(0.49-3.50)
		Current Smoker^	1 (13)	1.20	0.88	(0.12-11.91)
		Any Illicit Drug Use	2 (6)	0.63	0.56	(0.14-2.91)
		AUDIT score $\geq 20^{\Pi}$	3 (11)	1.00	0.99	(0.27-3.65)
Analysis 6	89 (44)	Heavy Drinker	22 (63)	1.31	0.48	(0.63-2.72)
		Current Smoker^	3 (11)	0.55	0.42	(0.13-2.33)
		Any Illicit Drug Use	6 (7)	0.66	0.43	(0.24-1.87)
		AUDIT score $\geq 20^{\Pi}$	10 (12)	1.34	0.54	(0.53-3.39)
Analysis 7	172 (86)	Heavy Drinker	41 (65)	3.01	0.10	(0.82-11.05)
		Current Smoker^	9 (15)	0.70	0.69	(0.12-3.94)
		Any Illicit Drug Use	17 (10)	1.00	-	-
		AUDIT score $\geq 20^{\Pi}$	10 (11)	3.69	0.21	(0.47-28.75)
Analysis 8	199 (99)	Heavy Drinker	44 (59)	1.00	-	-
		Current Smoker^	11 (16)	1.00	-	-
		Any Illicit Drug Use	17(9)	1.00	-	-
		AUDIT score $\geq 20^{\Pi}$	20 (11)	1.00	-	-

NOTES:
* OR calculated using non-missing values
^ Compared to never smokers
-: There were 0 persons in the comparison group and the OR could not be calculated.
∏ Compared to an AUDIT score <20.

Table 4a. The frequency of cluster membership among HIV-positive men who have sex with men and transgender women

Covariate	Cluster Analysis 1		Cluster Analysis 2		Cluster Analysis 6	
	No	Yes	No	Yes	No	Yes
Total	139 (69)	62 (31)	87 (43)	114 (57)	112 (56)	89 (44)
Age						
18-24	74 (53)	37 (60)	44 (51)	67 (59)	58 (52)	53 (60)
25-34	52 (38)	23 (37)	33 (38)	42 (37)	42 (38)	33 (37)
35+	13 (9)	2 (3)	10 (11)	5 (4)	12 (11)	3 (3)
Sexuality and Gender Identity						
MSM	119 (86)	59 (95)	71 (82)	107 (94)	97 (87)	82 (92)
TW	20 (14)	3 (5)	16 (19)	7 (6)	14 (13)	7 (8)
Sex Work						
No	123 (88)	56 (92)	75 (86)	104 (92)	97 (87)	82 (92)
Yes	16 (12)	5 (8)	12 (14)	9 (8)	14 (13)	7 (8)
Alcohol Consumption						
Not a heavy drinker	57 (66)	26 (65)	38 (69)	45 (63)	47 (68)	36 (62)
Heavy drinker	30 (34)	14 (35)	17 (31)	27 (37)	22 (32)	22 (38)
AUDIT Score						
≤20	117 (88)	49 (92)	74 (89)	92 (89)	95 (90)	71 (88)
≥20	16 (12)	4 (8)	9 (11)	11 (11)	10 (10)	10 (12)
Tobacco Consumption						
Never smoker	37 (76)	15 (68)	24 (72)	28 (74)	31 (72)	21 (75)
Current smoker	8 (16)	3 (14)	6 (18)	5 (14)	8 (19)	3 (11)
Former smoker	4 (8)	4 (18)	3 (9)	5 (14)	4 (19)	4 (14)
Illicit Drug Use						
No illicit drug use	126 (91)	58 (94)	77 (89)	107 (94)	101 (90)	83 (93)
Any illicit drug use	13 (9)	4 (6)	10 (11)	7 (6)	11 (10)	6 (7)
No marijuana use	128 (92)	58 (94)	78 (90)	108 (95)	102 (91)	84 (94)
Marijuana use	11 (8)	4 (6)	9 (10)	6 (5)	10 (9)	5 (6)
No popper use	133 (96)	62 (100)	82 (95)	113 (99)	107 (96)	88 (99)
Popper use	6 (4)	0 (0)	5 (6)	1 (1)	5 (4)	1 (1)
No cocaine use	135 (97)	62 (100)	83 (95)	114 (100)	83 (95)	114 (100)
Cocaine use	4 (3)	0 (0)	4 (5)	0 (0)	4 (5)	0 (0)

NOTES:
MSM: Men who have sex with men
TW: Transgender women

Table 4b. The odds of cluster membership among HIV-positive men who have sex with men and transgender women

	Cluster Analysis 1			Cluster Analysis 2			Cluster Analysis 6		
Covariate	**OR**	**P-value**	**95% (CI)**	**OR**	**P-value**	**95% (CI)**	**OR**	**P-value**	**95% (CI)**
Age									
18-24	ref.	-	-	ref.	-	-	ref.	-	-
25-34	0.88	0.70	(0.47-1.66)	0.84	0.55	(0.46-1.51)	0.86	0.62	(0.48-1.55)
35+	0.31	0.13	(0.07-1.43)	0.33	0.06	(0.11-1.03)	0.27	0.05	(0.07-1.02)
Sexuality and Gender Identity									
MSM	ref	-	-	ref.	-	-	ref.	-	-
TW	0.30	0.06	(0.09-1.06)	0.29	0.01	(0.11-0.74)	0.40	0.07	(0.15-1.07)
Sex Work*									
No	ref.	-	-	ref.	-	-	ref.	-	-
Yes	0.69	0.48	(0.24-1.97)	0.54	0.19	(0.22-1.35)	0.59	0.28	(0.23-1.54)
Alcohol Consumption*									
Not a heavy drinker	ref.	-	-	ref.	-	-	ref.	-	-
Heavy drinker	1.02	0.96	(0.47-2.24)	1.34	0.44	(0.64-2.82)	1.25	0.55	(0.60-2.61)
AUDIT Score*									
≤20	ref.	-	-	ref.	-	-	ref.	-	-
≥20	0.60	0.38	(0.19-1.88)	0.98	0.97	(0.39-2.50)	1.34	0.54	(0.53-3.39)
Tobacco Consumption*									
Never smoker	ref.	-	-	ref.	-	-	ref.	-	-
Current smoker	0.93	0.92	(0.22-3.97)	0.71	0.61	(0.19-2.64)	0.55	0.42	(0.13-2.33)
Former smoker	2.47	0.24	(0.22-3.97)	1.43	0.65	(0.31-6.61)	1.48	0.61	(0.33-6.57)
Illicit Drug Use									
No illicit drug use	ref.	-	-	ref.	-	-	ref.	-	-
Any illicit use	0.67	0.50	(0.21-2.14)	0.50	0.18	(0.18-1.38)	0.66	0.44	(0.24-1.87)
No marijuana use	ref.	-	-	ref.	-	-	ref.	-	-
Marijuana use	0.80	0.72	(0.25-2.63)	0.48	0.18	(0.16-1.41)	0.61	0.38	(0.20-1.85)
No popper use	ref.	-	-	ref.	-	-	ref.	-	-
Popper use	1	-	-	0.15	0.08	(0.02-1.27)	0.24	0.20	(0.03-2.12)
No cocaine use	ref.	-	-	ref.	-	-	ref.	-	-
Cocaine use	0	-	-	0	-	-	0	-	-

*OR calculated using non-missing values

Table 5: Model assessment for HIV onward transmission among HIV-positive men who have sex with men and transgender women

	Model 1			Model 2			Model 3			Model 4		
Covariate	**aOR**	**P-value**	**95% (CI)**	**aOR**	**P-value**	**95% (CI)**	**aOR**	**P-value**	**95% (CI)**	**aOR**	**P-value**	**95% (CI)**
Heavy Drinker	1.51^	0.30	(0.70-3.28)									
Current Smoker				0.41≅	0.23	(0.10-1.73)						
Any Illicit Drug Use							0.53Ω	0.23	(0.19-1.49)			
AUDIT Score ≥20										1.30Δ	0.61	(0.47-3.65)

NOTES:

**Cluster thresholds:* patristic distance 0.02, cluster size of ≥2 *Sabes* participants; odds ratio compares the odds of clustering amongst individuals who reported using binge drinking any illicit drug in the 30 days prior to HIV diagnosis, or currently smoking once they were HIV diagnoses, compare to individuals who did not report using those substances.

^ Model was adjusted for sexuality and gender.

≅ Model was adjusted for education level, and sexuality and gender

Ω Model was adjusted for sexuality and gender.

Δ Model was adjusted for sex work, education level, and sexuality and gender.