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Substance Use and Alcohol among Key Populations at risk for HIV: Novel Approaches in Intervention Development and Evaluation.

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Substance Use and Alcohol among Key Populations at risk for HIV: Novel Approaches in Intervention Development and Evaluation.

by

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DISSERTATION

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A version of Chapter 1 of this dissertation has been published online ahead of print in *Drug and Alcohol Review*.[1] Versions of Chapter 2 and 3 have been published online ahead of print in *Drug and Alcohol Dependence*.[2,3] The final co-authors listed in each publication directed and supervised the research that forms the basis for the dissertation chapters. The published material is substantially the product of Glenn-Milo S. Santos' period of study at UCSF and was primarily conducted and written by him. The work he completed for these published manuscripts are comparable to a standard dissertation chapter.

Approved: _____, David Vlahov, PhD, RN, Dissertation Chair

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Substance Use and Alcohol among Key Populations at risk for HIV:

Novel Approaches in Intervention Development and Evaluation.

Glenn-Milo S. Santos

Abstract

Substance use and alcohol can have negative health consequences among both HIV-positive and -negative individuals, and are associated with behaviors that facilitate HIV transmission and acquisition, particularly among key affected populations disproportionately impacted by HIV, including transgender women, men who have sex with men (MSM) and adults from sub-Saharan Africa. Although there is a large body of literature documenting the overlap between substance use, alcohol and HIV, many gaps remain in our understanding of these intertwined conditions. For example, the relationship between HIV infection and different classes and patterns of substance use and alcohol consumption remain understudied among transgender women. On the other hand, those relationships are well-characterized for non-dependent substance-using and alcohol-drinking MSM, yet there are no evidence-based behavioral interventions efficaciously shown to reduce substance use, alcohol and associated harm exclusively for this population. Furthermore, among treatment-naïve HIV-positive individuals, there is limited longitudinal data characterizing the impact of anti-retroviral treatment (ART) initiation on alcohol consumption. The objective of this dissertation was to address these gaps in the literature and help elucidate the complex interplay between substance use, alcohol consumption and HIV with a special emphasis on key affected populations. The study populations and study designs in this dissertation include: 1) transgender women from San Francisco (n=314) from a Respondent Drive Sampling (RDS) study conducted in 2010; 2) HIV-negative, sexually-active, substance-using and alcohol-drinking MSM from San Francisco (n=326) from a randomized controlled trial (RCT) on the efficacy of a behavioral intervention,

Personalized Cognitive Counseling (PCC), compared to rapid HIV testing to reduce HIV-related sexual risk behaviors conducted from 2009-2012; and 3) HIV-positive individuals from rural Uganda initiating ART (n=502) from a prospective cohort study followed from 2005-2011. The key findings of these studies are summarized below.

In the RDS study, transgender women who reported any methamphetamine use (AOR 3.02 (95%CI=1.51-6.02)), methamphetamine use before or during anal intercourse (AOR 3.27 (95%CI=1.58-6.77)), and at least weekly methamphetamine use (AOR 3.89 (95%CI=1.64-9.23)) had significantly greater odds of testing positive for HIV, compared to those who did not use methamphetamine. Consistent associations were observed in RDS-adjusted models using sampling weights that take into account the probability of being recruited into the study and similarities between network members (homophilly). This is the first study that has examined the relationship between alcohol and substance use, and HIV infection among transwomen in an RDS study, by substance class type and by frequency, using global and situational measures. This study observed that transgender women who tested positive for HIV significantly used more methamphetamine, in general, and in conjunction with sex. These findings highlight the critical need to develop interventions aimed at addressing both substance use and HIV risk among transgender women.

In the PCC trial, compared to MSM who received rapid HIV testing only, MSM randomized to PCC were more likely to report abstaining from alcohol consumption (RR=0.93; 95%CI=0.89-0.97), marijuana use (RR=0.84; 95%CI=0.73-0.98), and erectile dysfunction drug use (EDD; RR=0.51; 95%CI=0.33-0.79) over the 6-month follow-up in generalized estimating equation (GEE) models. PCC was also associated with significant reductions in frequency of alcohol intoxication (OR=0.58; 95%CI=0.36-0.90) over follow-up in ordered logistic regression models. Furthermore, PCC was associated with significant reductions in number of unprotected

anal intercourse events while under the influence of methamphetamine (RR=0.26; 95%CI=0.08-0.84). The addition of PCC to rapid HIV testing may have benefits in increasing abstinence from certain classes of substances previously associated with HIV risk, including alcohol and EDD; and reducing alcohol intoxication frequency and high-risk sexual behaviors concurrent with methamphetamine use. Of note, there was no evidence that PCC was efficacious in reducing the pre-specified primary sexual risk behavior outcomes in the overall sample of MSM in the trial. This is the first study to report significant reductions in alcohol and substance use associated with PCC, an intervention identified by the Centers for Disease Control and Prevention (CDC) as an evidence-based intervention for HIV-related sexual risk reduction among MSM. Findings from this study raise the possibility that PCC can affect HIV risk by reducing alcohol and substance use in this population.

In the cohort study with HIV-positive Ugandans, among the current drinkers, 90 (83.3%) reported first abstaining from alcohol for at least 90 days during follow-up. The majority (n=50) of those who abstained reported doing so by their 3-month visit. Additionally, 14 participants became abstinent by their 6-month visit and the 26 participants became abstinent by their 9-month visit or later. Among the 90 who abstained from alcohol for at least 90 days, 21 (23.3%) resumed drinking at some point during the course of the 6-year follow-up (4 relapsed at 6 month, 2 at 9 month, and 15 after 9 month visits). In the pooled logistic regression (PLR) analysis, alcohol abstinence was most likely to start immediately after ART initiation (AORs for 6 month versus 3 month visit: 0.25 [0.10-0.61]; 9 month visit or later versus 3 month visit: 0.04 [0.02-0.09]). Findings from the PLR model were consistent in a sensitivity analysis that imputed missing data using multiple imputation by chained equations (ICE), suggesting that these findings are robust. This study found that a large majority of HIV-positive alcohol drinkers starting ART reported becoming and remaining abstinent from alcohol consumption. This study provides insight on the longitudinal alcohol consumption patterns of HIV-infected adults initiating

ART and can inform the development of new alcohol interventions in sub-Saharan Africa, where hazardous alcohol consumption is common and additional evidence-based alcohol interventions outside large urban areas are needed. In particular, this study suggest that ART may have additional collateral effects on alcohol consumption and that ART initiation may be an opportune time to implement additional interventions for alcohol consumption—especially since many individuals relapse—and other health behaviors for this population.

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Chapter 1: Alcohol and Substance use Among Transgender Women in San Francisco: Prevalence and Association with HIV infection

Introduction

Male-to-female transgender women (transwomen) have a disproportionate burden of HIV worldwide.[1-3] In a meta-analysis of all available data, it is estimated that nearly one in five (19.1%) transwomen are HIV-positive and transwomen have 48.8 fold greater odds of being HIV-positive compared to the general adult population.[3] In the United States, meta-analyses of available biologic data estimate that 27% of transwomen are HIV-positive.[2] In San Francisco, an HIV consensus expert panel estimated that 35.5% of transwomen with no history of injection drug use (exclusive of hormone use) are HIV-positive.[4] Transwomen with HIV in San Francisco also have a significantly higher average aggregate viral load compared to San Francisco overall, suggesting that a greater proportion of transwomen are not receiving optimal HIV care.[5]

Alcohol and substance use are highly prevalent among lesbian, gay, bisexual, and transgender (LGBT) populations.[6-11] Although national population-based estimates are not available for transwomen, convenience samples of transwomen also suggest a high prevalence of alcohol and substance use.[12-15] The overlap between HIV and alcohol and substance use in other populations are well documented. [16-26] However, transwomen may be uniquely at risk for alcohol and substance use and HIV due to transphobia, stigma, discrimination, and stressful life-events.[27-29] Thus, prior findings on the association between alcohol and substance use and HIV might not be generalizable to transwomen.

Unfortunately, there is a scarcity of data on the prevalence and independent effects of different classes of substances on HIV infection among transwomen. In addition, many transwomen studies have assessed substance use in general (i.e. measures collapsed substance classes together).[30-32] The lack of specificity in these analyses is problematic because the strength of

association between HIV risk and different substances may vary by substance type.[16, 17, 33] Moreover, we are not aware of any studies that assessed the relationship between HIV status and frequency of substance use in this population; distinguishing between infrequent or "episodic" use and frequent use can demonstrate dose-response associations between substance use and risk for HIV, which may provide stronger support for causality. [16, 17, 21, 34]

The aims of this study were to address these gaps in knowledge by assessing the prevalence of alcohol and various classes of substances and evaluating the relationship with HIV infection in a Respondent Driven Sampling (RDS) study of transwomen in San Francisco. Another additional aim of this study was to assess the relationship between frequency of use and HIV infection. Based on prior findings on alcohol, substance use and HIV, we hypothesize that: 1) stimulants (including methamphetamine, powdered and crack cocaine) and alcohol would be more strongly associated with HIV infection compared to other classes of substances (e.g. non-stimulants); and 2) more frequent substance use would be associated with greater risk of HIV infection compared to less frequent or no use.

Methods

Study Sample and Recruitment

We conducted a cross-sectional study with 314 transwomen in San Francisco from August-December 2010 using RDS. The methodology of this study and the reliability of this study's sampling method are presented in greater detail elsewhere.[35] In brief, the study recruited 11 ethnically/racially diverse seeds, who made up the initial pool of participants enrolled to generate subsequent network referrals for the study, who were at least 18 years of age and identified as transwomen. Seeds and enrolled participants received coupons (3-5 each) to

recruit other transwomen into the study from their respective networks. Transwomen who enrolled in the study received a $50 stipend. In addition, participants received an additional $10 stipend for each network referral enrolled in the study. The coupon return rate was 36.8% and the average total stipend received by participants was $70. Among the 318 transwomen who were screened for eligibility, 95.3% were deemed eligible and agreed to participate. This study reached equilibrium (i.e., sample stability in the frequency distributions of key variables) and satisfied other ideal RDS criteria;[36, 37] for example, the study had many long recruitment chains (mean number of referrals between initial seeds and terminal members of the recruitment chain [i.e., waves] = 6; range = 1-15) and generally moderate homophily (i.e., the tendency of individuals to recruit people like themselves) with respect to race / ethnicity (range: 0.15-0.63). Information from a formative assessment suggested that networks of transwomen in San Francisco are strongly race-/ethnicity-based and this would play a key role in the sampling of diverse transwomen; thus, equilibrium was evaluated with respect to race / ethnicity. The study reached equilibrium by the seventh wave of recruitment.[35] Hence, RDS was demonstrated to be a suitable sampling method for this transwomen population. Transwomen enrolled in the study were interviewed face-to-face using a standardized questionnaire. All participants were also offered an HIV rapid antibody test. All study procedures received approval from the Committee on Human Research at the University of California San Francisco and all participants provided informed consent.

Measures

The study questionnaire collected information on demographic and social characteristics. The questionnaire also evaluated the use of various classes of substances separately, in the past 12 months, utilizing the same measures used in the National HIV Behavioral Surveillance (NHBS)(e.g. “How often have you used [substance class] in the past 12 months?”).[6] Substance classes evaluated include the following: methamphetamine, crack cocaine,

powdered cocaine, downers, painkillers, hallucinogens, and heroin, as well as club drugs including ecstasy, GHB, ketamine, and poppers. Club drug types were reported together because prevalence of their use was low. Substance use frequency was ascertained with response options including: “didn’t use”, “once a month or less”, “about once a week”, “several times a week”, “about once a day”, and “several times a day”. To evaluate dose-response associations, frequency of use was classified as no use, “episodic use” for less than weekly use, or at least weekly use (i.e. “about once a week” or greater). These classifications have been used in other substance studies in the literature.[16, 38] Substance use was also assessed with global (i.e. any use) and situational (i.e. “Did you use [substance class] before or during sex in the last 12 months?”) measures. These global and situational substance use classifications have been previously described in the literature.[39]

Outcome

The primary outcome of interest in the multivariable logistic regression analysis was HIV rapid antibody test result (HIV antibody positive or negative). Those who declined HIV testing were excluded from this analysis..

Data Analysis

We evaluated the global and situational associations between alcohol and substances that have been previously associated with HIV risk—alcohol, methamphetamine, powdered cocaine, crack cocaine, and club drugs—while adjusting for potential confounders including age, race/ethnicity, income, education, and history of injection drug use (IDU) in separate multivariable logistic regression models. Since the situational measures on substance use before or during anal intercourse were collinear with anal intercourse measures (correlation coefficient $p<0.001$), and because we were interested in the pathway between substance use and HIV infection via by sexual risk behaviors, we did not adjust for anal intercourse measures in our multivariable

model. We also evaluated the presence of a dose-response relationship between categories of substance use frequency, using non-use as the referent (i.e. non-use versus episodic, no-use versus at least weekly) and HIV infection using similar procedures. Additionally, to evaluate the effect of polysubstance use patterns (i.e., using multiple substances together or sequentially within a given period), we created a composite variable on the cumulative number of substances used, in general and in the context of anal intercourse, inclusive of methamphetamine, crack cocaine, powdered cocaine and club drugs. Multivariable logistic regression analyses included all participants tested for HIV; these analyses were conducted using STATA 12.0 (College Station, TX).

RDS-weighted analyses

We used RDS Analysis Tool 6.0 (RDSAT; Cornell, NY) to estimate the population prevalence and 95% confidence interval of various classes of substances and other descriptive findings, using sampling weights adjusted for homophily and network size of respondents (surrogate measures for probability of being recruited into the study). In the primary outcome analysis, we exported individual sampling weights for HIV-infection from RDSAT and evaluated the global and situational associations between substance measures of interest using established RDS weighted multivariable regression techniques, while adjusting for the same covariates in the unweighted multivariable analyses. In sensitivity analyses, we trimmed large sampling weights to be equal to the 90th percentile value and reran weighted analyses with trimmed weights.

Results

Sample Characteristics

As shown in **Table 1**, the mean age of transwomen in the study was 42 years old (standard deviation=10.9). The study was diverse: 30.6% were Latina/Hispanic, 28% were African

American, 6.7% were Asian Pacific Islander, 16.6% were Caucasian and 18.2% were other. Most transwomen (96.1%) did not have a college degree. The proportion of transwomen who reported being homeless was 9.2%.

HIV Prevalence and HIV-related Risk Behaviors

Among the 314 transwomen, 285 consented to having an HIV test. The prevalence of HIV infection was 35% among those tested. HIV prevalence by self-report was 31.5%. There were no statistically significant differences between transwomen who declined and those who consented to testing with respect to age, housing, relationship status, education, race/ethnicity, self-reported HIV status, and length of time since HIV diagnosis (p-values all >0.05)

Substance Use Patterns

Substance use within the past year was reported by 43.3% of the sample. The most common classes of substances used were: marijuana (29%), methamphetamine (20.1%), and crack cocaine (13.4%), as reported in **Table 2**. Club drugs were used by 13.1% of participants. In our sample, 58% of transwomen participants reported drinking alcohol in the past 6 months, and 29.9% reported five or more drinks in a single session ("binge drinking"). Over a quarter of transwomen (28%) reported using two or more substances, exclusive of alcohol (i.e. polysubstance use).

Over half of transwomen had been under the influence of any alcohol or substance before or during anal intercourse (51.3%), while the prevalence of unprotected anal intercourse while high or drunk was 16.6% (**Table 1**). In addition, the majority of transwomen who used alcohol, methamphetamine, cocaine, and club drugs reported using these respective substance classes before or during anal intercourse (**Table 2**)**.**

Unweighted Multivariable Analyses for HIV infection

The results of the multivariable logistic regression model examining the global, situational and dose-response associations between alcohol, substance use and HIV infection are summarized in **Table 3**.

Methamphetamine Use

Transwomen who reported methamphetamine use had significantly greater odds of testing HIV-positive, compared to those who didn't use methamphetamine (AOR=3.0; 95%CI=1.51-5.94). Additionally, transwomen who used methamphetamine before or during anal intercourse had significantly greater odds of testing HIV-positive, compared to those who did not use methamphetamine in the context of anal intercourse (AOR=3.26; 95%CI=1.59-6.69). The odds of testing HIV-positive were similar for non-users and episodic methamphetamine users. At least weekly methamphetamine users had greater odds of testing HIV-positive compared to non-users (AOR=3.63; 95%CI=1.55-8.50)**.**

Crack or Powdered Cocaine Use

Transwomen who reported using crack cocaine and powdered cocaine had similar odds of testing HIV-positive, compared to non-users. We did also not observe a significant association between using crack cocaine before or during anal intercourse and HIV infection. Transwomen who reported powdered cocaine use before or during anal intercourse had greater odds of testing HIV-positive, compared to those who did not use powdered cocaine in the context of anal intercourse (AOR=3.4; 95%CI=1.20-9.58). We did not observe a significant dose-response relationship for frequency of crack cocaine and powdered cocaine.

Club Drug Use

Using club drugs before or during anal intercourse was not significantly associated with testing HIV-positive for transwomen in the study. Those who used club drugs at least weekly were significantly more likely to test HIV-positive, compared to those who did not use club drugs (AOR=6.02; 95%CI=1.73-20.9).

Alcohol Use

As shown in **Tables 3**, we did not observe any significant differences in alcohol use and binge drinking patterns globally or situationally between HIV-positive transwomen and those who tested negative.

Polysubstance use

Compared to those who used no substances, those who reported using three or more substances had significantly greater odds of testing positive for HIV (AOR=6.2; 95%CI=1.47-26.1). Those who reported using two and three or more substances before or during anal intercourse had 2.66 (95%CI=1.15-6.16) and 4.43 (95%CI=1.35-14.56) fold greater odds of testing positive for HIV, respectively, compared to those who did not use any substances in the context of sex.

RDS-weighted Multivariable Analyses for HIV infection

The results of the RDS-weighted multivariable logistic regression model examining the global, situational and dose-response associations between alcohol, substance use and HIV infection are summarized in **Table 4**. In sensitivity analyses using weights trimmed to the 90th percentile, no substantial differences were noted in the results with respect to significance and magnitude of association.

Methamphetamine Use

In RDS-weighted analyses, transwomen who reported methamphetamine use had a 4.59 (95%CI=1.89-11.17) fold greater odds of testing positive for HIV, compared to those who didn't use methamphetamine. Additionally, transwomen who used methamphetamine before or during anal intercourse had 4.8 (95%CI=1.9-12.13) greater odds of testing positive for HIV, compared to those who did not use methamphetamine in the context of sex. Furthermore, we observed a significant dose-response relationship between frequency of methamphetamine use and HIV-status. Compared to non-users, episodic methamphetamine users and at least weekly methamphetamine users had a 4.25 (95%CI 1.3-13.92) and 4.79 (95%CI=1.58-14.5) fold greater odds of testing positive for HIV.

Crack or Powder Cocaine Use

In weighted analyses, transwomen who reported using powdered cocaine had 4.22 (95%CI=1.32-13.54) fold higher odds of testing positive for HIV, compared to those who did not use powdered cocaine. Transwomen who reported powdered cocaine use before or during anal intercourse also had greater odds of testing positive for HIV (AOR 5.98; 95%CI=1.54-23.26), compared to those who did not use powdered cocaine before or during anal intercourse. At least weekly powdered cocaine use was significantly associated with testing positive for HIV (AOR=87.37; 95%CI=7.62-1001.61). We did not observe a significant association between using crack cocaine in general, and using crack cocaine before or during anal intercourse and HIV infection. We did not observe a significant dose-response relationship between frequency of either crack cocaine and testing positive for HIV.

Club Drug Use

In weighted analyses, we did not observe a significant association between using club drugs and using club drugs before or during anal intercourse and testing positive for HIV. At least weekly club drug use was significantly associated with testing positive for HIV (AOR=11.25; 95%CI=2.78-45.48).

Alcohol Use

As shown in **Table 4**, we did not observe any significant differences in alcohol use and binge drinking patterns globally or situationally between HIV-positive transwomen and those who tested negative for HIV in weighted analyses.

Polysubstance use

Compared to those who used no substances, those who reported using two and three or more substances had significantly greater odds of testing positive for HIV (AOR=6.98; 95%CI=2.27-21.44; AOR=4.75; 95%CI=1.24-18.26, respectively). Those who reported using one, two and three or more substances before or during anal intercourse had 3.3 (95%CI=1.26-8.6), 3.77 (95%CI=1.10-12.9), and 8.04 (95%CI=1.39-46.42) fold greater odds of testing positive for HIV, respectively, compared to those who did not use any substances in the context of sex.

Discussion

In this study of transwomen sampled using RDS methods, we observed a high prevalence of substance use. The prevalence of substance use that we observed in this study was greater in this group compared to what has been previously found in the general population. In the 2009 United States National Drug Household Survey, the past year prevalence of any illicit

substance, marijuana, methamphetamine, powdered cocaine and crack cocaine use were 14.4%, 10.1%, 0.5%, 2.3%, 0.6%, respectively.[40] In contrast, our sample found that 43.3% of transwomen had used any substances in the past 12 months; 29% used marijuana; 20.1% used methamphetamine; 8.3% used powdered cocaine; and 13.4% used crack cocaine. In addition, we note that the majority of substance-using transwomen in this study reported substance use within the context of anal intercourse. The majority of transwomen in this study reported substance use within the context of sex, a finding that has been observed in studies of MSM.[6] Notably, we observed low prevalence of poppers use (<10%) among transwomen. This is a striking difference relative to many samples of MSM, among whom poppers use—and associated HIV risk from poppers use—is well documented.[17, 21] And although binge-drinking has often been associated with HIV risk among MSM, we did not observe this association among transwomen.[33] The prevalence of binge-drinking in the study is modest (<30%) relative to findings observed in samples of MSM (e.g. 57% of MSM are current binge-drinkers in the NHBS).[41] It is possible that we did not have the power to detect an association in our sample. The lower prevalence of alcohol and some classes of substance use among transwomen compared to MSM may indicate differences in preferences or norms pointing to the cultural divide between transwomen and MSM. Protective factors related to gender identity may also be at play. For example, transwomen on hormone therapy may be worried about contraindications with their prescribed medications and adverse effects on their gender identity as a result of drug use. However, more research is needed to fully elucidate the reason for these differences. Qualitative studies exploring motivations, preferences or patterns of alcohol and substance use among transwomen may assist in explaining these findings. Notably, these findings underscore the need to collect disaggregated data on substance use measures for key populations like transwomen as the patterns of consumption and prevalence are different from other currently studied populations like MSM.

Among all the classes of substances we evaluated, methamphetamine appears to be the drug that is most strongly associated with HIV infection, independent of education, income and IDU history. Specifically, we found that global methamphetamine use, methamphetamine use before or during anal intercourse, and at least weekly methamphetamine use were positively and significantly associated with testing HIV-positive. The point estimates for methamphetamine also stood out in these analyses because they were large in magnitude; all significant methamphetamine measures were associated with over 3 fold greater odds of testing HIV-positive. The consistent findings across these methamphetamine measures suggest that these results are robust. We did not find compelling evidence that powdered cocaine, crack cocaine, club drug use, and alcohol were independently associated with HIV infection among transwomen in this study. For these substances, we observed isolated findings that were not consistent across global, situational, and dose-response analyses. Additionally, in both global and situational analyses in unweighted and weighted models, we found that those who reported using three or more substances, in general and in the context of sex, had consistently significantly greater odds of testing positive for HIV. These findings point to the need to develop interventions that can jointly reduce harm from multiple substances, especially since polysubstance use was associated with greater risk for HIV. To our knowledge, this is the first study that has examined the relationship between alcohol and substance use, and HIV infection among transwomen in an RDS study by substance class type and frequency, using global and situational measures.

This study has several limitations. First, this study was cross-sectional in design, which limits our ability to make causal inferences. We did not ascertain temporality between alcohol and substance use, and HIV infection. It is plausible that transwomen are using methamphetamine as a result of their HIV infection; some HIV-positive individuals may use methamphetamine for

HIV-related pain or fatigue.[42] It is also unclear why powdered cocaine use during anal intercourse was associated with testing HIV-positive, while crack cocaine use during anal intercourse was not. Crack cocaine is associated with HIV disease progression and higher rates of AIDS-related mortality among women.[25, 43] Thus, it is possible that crack-cocaine-using transwomen living with HIV are sicker and have higher mortality rates, resulting in a selection bias that may bias our results toward the null. In addition, there is greater stigma against crack cocaine compared to powdered cocaine use [44] and although these substances are pharmacologically similar, penalties for crack cocaine are generally more severe.[45] Thus, it is likely that under-reporting for crack cocaine is more common than powdered cocaine, which may have also biased our results toward the null.

Nevertheless, our findings have important public health implications because substance use can have negative health consequences among both HIV-positive and -uninfected individuals and it is associated with behaviors that lead to HIV transmission/acquisition.[29, 30, 32] Moreover, for HIV-positive individuals, substance use has been associated with poorer ART adherence, HIV-related health outcomes and less optimal care.[18, 20, 22-26, 46] In addition, because our point estimates for at least weekly use methamphetamine and club drugs, and cocaine use before or during anal intercourse, had wide confidence intervals, these findings should be interpreted with caution. Moreover, although our primary outcome is an objective measure, our substance use data may be subject to measurement bias. We also cannot rule out the possibility of unmeasured confounders in this observational study. For example, the study did not measure risk-taking personality, impulsivity or sensation-seeking traits, which have been associated with both increased substance use and greater risk for HIV infection. Case-crossover analyses using event-level data on substance use and HIV-risk are considered the gold-standard in the literature because they can rule-out the effect of these within-subject characteristics,

Unfortunately, this study did not collect event-level data on these measures. Future studies among transfemales should endeavor to measure event-level data, whenever possible.

In addition, we do not assume that the transwomen in the study are representative of all transwomen in San Francisco. In an attempt to take into account potential selection bias that may have resulted from the sampling methods of RDS, we conducted weighted analyses using sampling weights adjusted for homophily and probability of being recruited into the study using established RDS methods.[47] The methods and results for weighted analyses are presented in detail in **Table 4**. The RDS-weighted analyses for methamphetamine measures yielded estimates consistent with unweighted analyses, with respect to magnitude (i.e. weighted models also estimated over 3 fold greater odds of testing HIV-positive for methamphetamine measures) and significance, suggesting that those associations are robust.

However, we observed different point estimates between the weighted and unweighted analyses for crack cocaine, powdered cocaine, and club drug measures. In particular, the weighted analyses found that global use of these substances were significantly associated with testing HIV-positive, associations which were not observed in the unweighted models. Theoretically, RDS-weighted results may yield representative findings that can be used for inferences to the larger population of transwomen in San Francisco, if the assumptions of RDS are met.[47] However, previous empirical comparisons of RDS studies with other sampling methods (e.g. quasi-population based Time Location Sampling strategies) among other hard to reach populations suggest that RDS studies may access only certain sub-populations of the population of interest (e.g. low-income).[48, 49] In some cases, weighted analyses were observed to have more biased estimates compared to unweighted analyses.[50] In our case, it is unclear if the unweighted or weighted findings are more representative of the larger transwomen population in San Francisco because data from non-convenience samples of

transwomen are not available for comparison. Additional surveillance studies among transwomen that utilize alternate sampling methods would provide points of comparison for determining whether weighted or unweighted analyses in this study would yield estimates that are more reflective of San Francisco's transwomen population. Ultimately, because our sample was limited to the San Francisco Bay Area, our findings (weighted or unweighted) are also not generalizable to transwomen in other geographic areas.

Despite these limitations—and given the overall paucity of data on transwomen—these findings provide data to consider in program planning for organizations working with transwomen, as well as areas of future inquiry for researchers in other geographic areas. This study also calls attention to the need for robust assessments of substance use and how use of these substances may be associated with HIV risk in this population. The associations we observed between substance use measures—particularly methamphetamine use—and HIV infection may warrant further examination. Longitudinal studies among transwomen that collect data on substance use are also needed to examine long-term trajectories of different classes of substance use and their possible contributions to HIV seroconversion. Among HIV-positive transwomen, the role of substances on HIV-related outcomes also needs further investigation. In summary, we found that transwomen in this sample have a high prevalence of alcohol and substance use. HIV-positive transwomen had higher odds of using methamphetamine, both generally and during anal intercourse. Given the disproportionate prevalence of HIV and substance use in this population, interventions aimed at addressing both substance use and HIV risk among transwomen are urgently needed.

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Table 1. Demographic, Behavioral and Clinical Characteristics of Transwomen (N=314) in San Francisco, 2010

		RDS-weighted		
		Crude %	**Adjusted %**	**95% CI**
Demographic				
Years of Age, mean (standard deviation)		42 (10.9)	-	-
Race/Ethnicity				
	African American	28.0	23.0	(14.3-32.3)
	Latina/Hispanic	30.6	38.1	(25.7-50.7)
	Caucasian	26.1	27.5	(20.4-36.8)
	Other	15.3	13.3	(6.6-18.6)
Education				
	Less than High School	26.8	30.6	23.6-36.3
	High School	63.1	62.2	55.5-69.6
	Some College	7.3	4.5	2.4-7.2
	College Graduate or beyond	2.9	2.8	0.9-5.3
Annual Income, US dollars				
	<21,000	83.8	86.5	81.9-90.9
	21-39,999	13.4	11.2	7.4-16.3
	40-50,000	2.2	1.5	0.1-3.1
	51-75,000	0.3	0.4	0-0.9
	>75,000	0.3	0.4	0-1.1
Housing Status				
	Homeless/Living in a shelter	9.2	11.6	(6.8-15.6)
	With stable housing	90.8	88.4	(84.4-93.2)
Employment				
	Unemployed	73.2	78.7	(73.2-83.1)
	Employed	26.8	21.3	(16.9-26.8)
Living openly as female full-time				
	No	9.2	11.8	(7.0-16.6)
	Yes	90.8	88.2	(82.5-93.5)
Residence				
	Bay Area (Non-San Francisco) Resident	8.6	7.4	(3.4-12.5)
	San Francisco Resident	91.4	92.6	(87.5-96.6)
Behavioral and Clinical				
*Any substance use**		43.3	41.4	(34.3-49.1)
*Any anal intercourse concurrent with alcohol and/or substance use**		51.3	48.4	(42.2-56.2)
*Any unprotected anal intercourse**		29.3	29	(22.3-37.7)
*Any unprotected anal intercourse concurrent with alcohol and/or substance**		16.6	15.4	(11.6-21.4)
Tested positive for HIV antibodies		31.5	36.2	(29.0-45.3)
Self-reported being HIV-positive		35	39.5	(31.8-47.8)
*Access alcohol or substance use treatment services**		15.6	18.3	(12.0-25.2)

Note: * recall period within past year

Table 2. Patterns of Alcohol (Past 6 months) and Substance use (Past 12 months) Among Transwomen in San Francisco, 2010

		Crude		RDS-weighted Prevalence Adjusted	
		(N=314)	%	%	(95-CI%)
Methamphetamine	*no*	251	(79.9)	78.4	(72.4- 85.6)
	yes	63	(20.1)	21.6	(14.4- 27.6)
	yes, before or during anal intercourse	52	(16.6)	18.5	(11.6- 24.3)
Crack Cocaine	*no*	272	(86.6)	85.7	(80.4- 89.7)
	yes	42	(13.4)	14.3	(10.0- 19.5)
	yes, before or during anal intercourse	24	(7.6)	7.1	(3.70- 11.1)
Powdered cocaine	*no*	288	(91.7)	92.1	(89.1- 94.6)
	yes	26	(8.3)	7.9	(5.40- 10.9)
	yes, before or during anal intercourse	19	(6.1)	5.8	(3.20- 9.10)
Club Drugs§	*no*	273	(86.9)	85.7	(82.2- 90.7)
	yes	41	(13.1)	14.3	(9.20- 17.7)
	yes, before or during anal intercourse	33	(10.5)	12.8	(7.40- 17.3)
Downers	*no*	297	(94.6)	93.5	(89.8- 96.4)
	yes	17	(5.4)	6.5	(3.60- 10.2)
	yes, before or during anal intercourse	4	(1.3)	1.2	(0.01- 2.80)
Painkiller	*no*	296	(94.3)	95.4	(92.5- 97.6)
	yes	18	(5.7)	4.6	(2.40- 7.50)
	yes, before or during anal intercourse	5	(1.6)	0.9	(0.20- 2.00)
Hallucinogens	*no*	309	(98.4)	98.3	(96.6- 99.5)
	yes	5	(1.6)	1.7	(0.50- 3.40)
	yes, before or during anal intercourse	1	(0.3)	0.4	(0.40- 1.70)
Heroin	*no*	304	(96.8)	97.3	(95.5- 98.7)
	yes	10	(3.2)	2.7	(1.30- 4.50)
	yes, before or during anal intercourse	7	(2.3)	2.0	(0.60- 3.90)
Marijuana	*no*	223	(71.0)	75.2	(69.9- 80.2)
	yes	91	(29.0)	24.8	(19.8- 30.1)
	yes, before or during anal intercourse	62	(19.8)	18.1	(13.5- 24.2)
Alcohol	*no*	132	(42.0)	43.1	(33.2- 49.5)
	yes	182	(58.0)	56.9	(50.5- 66.8)
	yes, before or during anal intercourse	101	(32.2)	31.4	(25.5- 40.3)
Binge Drinking	*no*	220	(70.1)	70.4	(62.5- 76.5)
	yes	94	(29.9)	29.6	(23.4- 37.3)
	yes, before or during anal intercourse	(not	collected)		

Note: Club Drugs is defined as ecstasy, GHB, ketamine and/or poppers

Table 3. Multivariable Logistic Regression Models: Alcohol/Substance use and HIV infection Among Transwomen in San Francisco, 2010*

Global substance use and testing positive for HIV					Situational substance use and testing positive for HIV				Substance use frequency and testing positive for HIV			
		AOR[a]	(95% CI)	p-value			**AOR[a]**	(0.95-CI)	p-value		**AOR[a]**	(0.95-CI)	p-value
Any methamphetamine		3.0	1.51-5.94	.002	Methamphetamine before or during anal intercourse		3.26	1.59-6.69	.001	Episodic methamphetamine	2.33	0.9-6.01	.08
										At least weekly methamphetamine	3.63	1.55-8.5	.003
Any crack cocaine		1.48	0.72-3.05	.284	Crack cocaine before or during anal intercourse		1.2	0.48-2.96	.695	Episodic crack cocaine	1.31	0.53-3.22	.553
										At least weekly crack cocaine	1.78	0.6-5.29	.297
Any powdered cocaine		2.27	0.92-5.59	.075	Powdered cocaine before or during anal intercourse		3.4	1.2-9.58	.021	Episodic powdered cocaine	1.66	0.6-4.6	.331
										At least weekly powdered cocaine	7.61	0.8-72.49	.077
Any club drugs[b]		1.93	0.9-4.1	.089	Club drugs[b] before or during anal intercourse		2.02	0.9-4.53	.089	Episodic club drugs	.91	0.35-2.41	.856
										At least weekly club drugs[b]	6.02	1.73-20.9	.005
Any alcohol		1.03	0.59-1.8	.908	Alcohol before or during anal intercourse		1.14	0.66-1.99	.637	Moderate alcohol	1.15	0.63-2.1	.645
										Heavy alcohol	0.88	0.38-2.04	.763
Any binge drinking		1.02	0.58-1.77	.954			(not	collected)			(not	collected)	
No. of substances§:	One	1.63	0.83-3.22	0.159	No. of substances used before or during anal intercourse §:	One	0.91	0.44-1.89	0.797				
	Two	2.37	0.82-6.88	0.112		*Two*	2.66	1.15-6.16	0.022		-	-	
	Three or more	6.2	1.47-26.1	0.013		*Three or more*	4.43	1.35-14.56	0.014				

*Notes:*Includes all transwomen who consented to HIV rapid antibody test; a= Model adjusted for age, race/ethnicity, income, education, and history of injection drug use; b= Club Drugs is defined as ecstasy, GHB, ketamine and/or poppers;* §=cumulative number of substances reported inclusive of methamphetamine, crack cocaine, powdered cocaine and club drugs used in general or before/during sex.

Table 4. RDS-weighted Multivariable Logistic Regression Models: Alcohol/Substance use and HIV infection among Transwomen in San Francisco, 2010*

Global substance use and testing positive for HIV					Situational substance use and testing positive for HIV				Substance use frequency and testing			
		AOR[a]	(95% CI)	p-value		**AOR[a]**	(0.95-CI)	p-value		**AOR[a]**	(0.95-CI)	p-value
Any methamphetamine		4.59	1.89-11.17	.001	Methamphetamine before/during sex	4.8	1.9-12.13	.001	Episodic methamphetamine	4.25	1.3-13.92	.017
									At least weekly methamphetamine	4.79	1.58-14.5	.006
Any crack cocaine		2.06	0.85-4.99	.109	Crack cocaine before/during sex	1.87	0.66-5.33	.24	Episodic crack cocaine	1.98	0.69-5.68	.207
									At least weekly crack cocaine	2.19	0.54-8.94	.274
Any powdered cocaine		4.22	1.32-13.54	.015	Powdered cocaine before/during sex	5.98	1.54-23.26	.01	Episodic powdered cocaine	2.57	0.73-9.02	.142
									At least weekly powdered cocaine	87.37	7.62-1001.61	0.001
Any club drugs[b]		2.24	0.92-5.44	.075	Club drugs[b] before/during sex	2.22	0.89-5.59	.089	Episodic club drugs	0.88	0.3-2.57	.815
									At least weekly club drugs[b]	11.25	2.78-45.48	.001
Any alcohol		1.02	0.51-2.04	.96	Alcohol before/during sex	0.99	0.49-2.01	.974	Moderate alcohol	1.38	0.64-3.0	.41
									Heavy alcohol	1.21	0.47-3.14	.693
Any binge drinking		0.94	0.47-1.87	.851		(not collected)				(not collected)		
No. of substances used§:	One	0.99	0.4-2.47	0.978	No. of substances used before or during anal intercourse§:	One	3.3	1.26-8.6	0.015	-	-	
	Two	6.98	2.27-21.44	0.001		*Two*	3.77	1.1-12.9	0.034			
	Three or more	4.75	1.24-18.26	0.023		*Three or more*	8.04	1.39-46.42	0.02			

Notes: Includes all transwomen who consented to HIV rapid antibody test; a= model adjusted for age, race/ethnicity, income, education, and history of injection drug use; b= club drugs is defined as ecstasy, GHB, Ketamine and/or poppers;* §=cumulative number of substances reported inclusive of methamphetamine, crack cocaine, powdered cocaine and club drugs used in general or before/during sex.
In sensitivity analysis, trimming sampling weights to the 90% percentile value resulted in similar results with respect to significance and magnitude of association (data not shown).

Chapter 2: Substance Use and Drinking Outcomes in Personalized Cognitive Counseling Randomized Trial for Episodic Substance-using Men who have sex with Men

Introduction

Alcohol and substance use are prevalent among men who have sex with men (MSM). Based on National HIV Behavioral Surveillance (NHBS) data, 42% of MSM used substances recreationally in the past year [1]. Moreover, National Household Survey on Drug Abuse (NHSDA) data show that MSM have higher lifetime prevalence of substance use and higher prevalence of "dysfunctional" use (i.e., having any symptoms of drug dependence) relative to other men in the United States [2]. NHBS data also suggest that among MSM, heavy episodic drinking ("binge-drinking"), defined as having five or more drinks on a single occasion, among MSM exceed rates reported for the general population [3, 4].

It is important to note, however, that most alcohol/substance-using MSM (SUMSM) do not meet criteria for dependence [5, 6]; only 5.7% of MSM have drug dependence syndrome in NHSDA [2]. Nevertheless, alcohol/substance use have important public health implications in their own right: 4.8% of the global burden of disease and 2.9 million deaths attributed to alcohol and drug use in 2010[7]. Moreover, use of alcohol/substances are independently associated with HIV-related sexual risk behaviors, as well as HIV seroconversion among MSM [8-12]. This may be compounded by the limited number of evidence-based behavioral interventions for non-dependent substance users; none of which are efficacious among MSM [13]. Although brief behavioral interventions, such as motivational interviewing have shown promise in addressing substance and alcohol abuse in the general population [14-17], efficacy of brief interventions is less compelling among MSM [18, 19]. Given the high prevalence of non-dependent substance use patterns among MSM, there is a great need to develop brief interventions that may be more suitable to this population than traditional intensive treatment programs for abuse/dependence.

We previously reported that the evidence-based Personalized Cognitive Counseling (PCC) intervention [20], adapted for episodic SUMSM [21], was not efficacious in reducing the pre-specified primary sexual risk behavior outcomes in the overall sample of MSM in the trial but was associated with significant reductions in number of unprotected anal intercourse (UAI) events with most recent non-primary partners among a subgroup of non-dependent participants [22], compared to rapid HIV testing only. As a secondary data analysis, we sought to evaluate whether PCC added to rapid HIV testing had collateral effects on alcohol/substance use outcomes among episodic SUMSM.

Methods

Study Design

This is a secondary data analysis testing the efficacy of PCC in reducing alcohol and substance use outcomes. The study, Project ECHO, was conducted in San Francisco, CA from May 2010-May 2012 (clinicaltrials.gov=NCT01279044; trial ended when target enrollment accrued and planned 6-month follow-up completed). Study procedures were approved by the institutional review board for the University of California, San Francisco.

Study methods have been reported elsewhere [22]. Briefly, 326 HIV-negative, SUMSM, ≥ 18 years old, were randomized 1:1 (using sequentially numbered opaque envelops from a computer-generated allocation sequence provided by an offsite statistician) by research associates to PCC adapted for SUMSM [21] or control, and followed at 3 and 6 month visits (see **Figure 1**). SUMSM were eligible if they reported no more than episodic use (defined as less than weekly use [5]) within two hours before/during sex of one of the following target substances previously identified as drivers of HIV risk among MSM: methamphetamine,

cocaine/crack, amyl nitrite ("poppers"), and binge-drinking. Sample size of 326 was determined based on parameters for primary outcomes of the trial [22].

PCC sessions were delivered at baseline, with booster sessions at 3-month visits. PCC involved discussion of participants' self-justifications (e.g. "Alcohol and/or drugs make it easier to have sex…") to minimize known risks during a recent UAI event while intoxicated from alcohol/substances. Sessions were tailored to specific substances and UAI events reported. Counselors also explored strategies to avoid future similar high-risk situations ([20, 23]. Rapid HIV testing was conducted at all visits.

Data Collection/Analysis

Self-reported alcohol/substance use was collected using audio computer-assisted self-interview (ACASI) with a 90-day recall period for all visits. The severity of dependence scale (SDS) for our target substances was also measured [24, 25]. Event-level data were collected on substances used within 2 hours before/during UAI events [5, 26]. We analyzed between group differences by intention-to-treat, without any regard to adherence to study procedures, but did not impute missing outcomes. We used generalized estimating equations (GEE) models to evaluate group-specific linear trends outcomes across the three study visits, with robust standard errors to account for within-subject correlation as well as potential over-dispersion of count outcomes. Binary and count outcomes were examined using Poisson and negative binomial models, respectively, while ordinal outcomes including SDS, frequency of alcohol intoxication (i.e. being "drunk or buzzed"), and frequency of substance use were assessed using the proportional odds/ordered logistic regression model. In all models, the effect of the intervention was estimated by the interaction between the treatment assignment indicator and a linear term in time. The exponentiated coefficient for interaction in the Poisson and negative binomial models is interpretable as the ratio of the intervention and control rates of change in the mean value of

the outcome, or rate-ratio (RR). We checked for imbalances at baseline, departures from linear trends, and violations of the proportional odds assumption. Analyses were conducted with STATA 12.0 (College Station, TX).

Results

The study recruited a diverse sample of 326 SUMSM (47% white, 26% Latino/Hispanic, 11% Asian/Pacific Islander, 10% black/African American, and 6% mixed/other race). Mean age was 33.6 years, and 71% attended some/finished college. Participant baseline characteristics in the two arms were similar (see **Table 5**).

Alcohol/Substance use prevalence

At baseline, the most common substances used were marijuana (61.7%), cocaine (32.5%), ecstasy (22.4%), erectile dysfunction drugs (EDD; 18.7%), prescription drugs (11.3%), methamphetamine (9.5%) and GHB (7.4%). Nearly all study participants reported consuming alcohol (96.6%). The mean number of binge-drinking days in the past 90 days for SUMSM in the study was 8.8 (standard deviation [SD] 9.26). Additionally, the mean number of UAI events while under the influence of alcohol overall was 2.3 (SD=2.9), while the mean number of events under the influence of poppers, cocaine and methamphetamine were 0.8 (SD=1.7), 0.3 (SD=1.0), and 0.2 (SD=1.2), respectively. A summary of substance use patterns among the two study conditions at baseline and over the course of the study is presented in **Table 6**. There were 3 and 11 of participants lost to follow-up in the control and PCC groups. In intention-to-treat analysis, 164 control and 162 PCC participants were included, regardless of adherence to group assignment. There were no study related adverse events.

Changes in substance use

A greater proportion of men in PCC abstained from alcohol, marijuana, and EDD during follow-up (**Figure 2**). Men who received PCC reported a 5% decline in alcohol consumption from baseline to 6-month visit (from 96% to 91%); while men in the control condition reported a 1% increase. There was also an 11% reduction in marijuana use from 63% at baseline to 56% at the 6-month visit in the PCC condition and a 4% increase in the control condition. Furthermore, among men in PCC, there was a 41% decline in EDD use, from 22% at baseline to 13% at the 6-month visit; and a 5% increase in the control condition. We did not observe significant differences in prevalence of GHB, methamphetamine, poppers, cocaine and prescription drug use between the study conditions. There were also no significant differences in number of binge-drinking days by study arm.

In intention-to-treat analysis, PCC participants reported significantly greater rates of abstinence from alcohol (RR=0.93; 95% confidence interval (CI)=0.89-0.97), marijuana (RR=0.84; 95%CI=0.73-0.98) and EDD (RR=0.51; 95%CI=0.33-0.79), than controls. In addition, PCC participants reported greater declines in mean number of UAI events while under the influence of methamphetamine (RR=0.26; 95%CI=0.08-0.84) and significantly greater reductions in alcohol intoxication frequency (OR=0.54; 95%CI=0.34-0.85). There were also no significant differences in the frequency of use for methamphetamine, poppers, cocaine by study arm.

Discussion

We observed significant intervention effects for several substance use outcomes. Specifically, abstinence from alcohol, marijuana, and EDD significantly increased while frequency of alcohol intoxication, as well as UAI events while intoxicated with methamphetamine significantly decreased among men receiving PCC, compared to controls. These intervention effects occurred among episodic SUMSM not seeking treatment to stop or reduce their substance use,

but interested in participating in a study to reduce HIV-related sexual risk behaviors while under the influence of alcohol/substances. To our knowledge, this is the first study to report significant reductions in alcohol/substance use associated with PCC, identified by CDC as an evidence-based intervention for HIV-related sexual risk reduction among MSM [13]. Findings from this study raise the possibility of adapted PCC to affect HIV risk by reducing alcohol/substance use.

The finding that a brief behavioral intervention can effectively reduce alcohol consumption among MSM is broadly consistent with another study that observed motivational interviewing alone can lead to significant reductions in drinking among MSM [27]. We observed declines in UAI while intoxicated with methamphetamine in the PCC arm, but did not find significant effects on methamphetamine use. The finding that a behavioral intervention can reduce methamphetamine-related sexual risk behaviors in the context of ongoing methamphetamine use is broadly consistent with results from prior randomized intervention trials among methamphetamine users [28, 29]. Collectively, these data support the feasibility of harm reduction strategies among methamphetamine users who may not be willing or able to abstain from use. However, our findings remain preliminary and additional studies are needed.

Although the increase in alcohol and marijuana abstinence associated with PCC in this study were modest, given the ubiquity of these two substances among SUMSM and the low-cost/low-resource attributes of PCC [30], this counseling approach may be a cost-effective, population-level intervention, if further proven effective [20, 23]. Furthermore, the significant effect of PCC on reducing frequency of alcohol intoxication corroborates the finding on alcohol abstinence and further suggests that these findings are robust.

Additionally, it is important to note the clinical significance and public health implications of PCC's effect on frequency of alcohol intoxication, recreational use of EDD and number of UAI

events while under the influence of methamphetamine, because these behaviors have been linked to risk of HIV acquisition and transmission among MSM [31-34]. In this study, PCC had medium to large effect sizes [35, 36] on these HIV-related risk factors (46%, 49% and 74% reductions for odds of alcohol intoxication frequency, rate of EDD use and rate of UAI concurrent with methamphetamine use, respectively); the magnitude of these estimates may portend to clinically significant intervention effects on these outcomes. Given the paucity of interventions for this non-dependent population, efforts to replicate these findings and adapt PCC to directly address these target substances may also be worthwhile.

It is unclear how a brief intervention, such as PCC, resulted in significant effects in some alcohol and substance use outcomes by 6-months. PCC sessions, though brief, may facilitate meaningful explorations of the self-justifications for risky behavior and motivate SUMSM to reducing their alcohol/substance use as a strategy to reduce their HIV-risk. Indeed, as reported in the primary outcome analyses, 6 of the 15 most frequently reported self-justifications for recent UAI in this study were alcohol/substance-related [22]. However, it is unclear why the intervention was effective for some substances, but not others. Additionally, it's unclear why some substances increased in the control group, though this may reflect the natural history of substance use (e.g. progression from recreational use to abuse, and then to dependence). Future studies are needed to fully elucidate the mechanism that contributed to these findings, and qualitative interviews may help pin-point ways to adapt PCC further to explicitly target alcohol/substance use outcomes.

This analysis has limitations. Outcomes were assessed through self-report. Although we used ACASI, some participants may have under-reported their use due to social desirability. Our study was limited to episodic SUMSM from San Francisco, and may not be generalizable to other populations. In addition, given the exploratory nature of this secondary data analysis, we

did not formally adjust for multiple comparisons; thus, findings of nominal statistical significance should be interpreted with caution. Finally, the finding that PCC was not efficacious in reducing sexual risk behaviors in the sample of MSM with symptoms of dependence in the trial [22] suggests that it may have limited potential as an HIV-prevention strategy among substance-dependent MSM.

Despite these limitations, future investigations on the effect of PCC on substance use would be of public health importance to cautiously confirm these exploratory findings, given the paucity of brief behavioral interventions for non-dependent substances users and acceptability of PCC among MSM [20]. This study found preliminary evidence that PCC was beneficial in stopping or reducing substance use, including alcohol, marijuana, and EDD, and concurrent use of methamphetamine with high-risk sexual behaviors. These behaviors are common and strongly associated with risk for HIV among SUMSM.

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Table 5. Sample Characteristics of Substance-Using MSM in Project ECHO Study, San Francisco 2010-2012

	Control N=164	(%)	PCC N=162	(%)	P-value §
Demographics					
Age, *mean (SD)*	33.2	(9.6)	34	(10.5)	0.56
Race/ethnicity					0.45
White	71	(44)	82	(51)	
Black	14	(9)	17	(11)	
Latino/Hispanic	48	(29)	38	(24)	
Asian and Pacific Islander	21	(13)	14	(9)	
Other	9	(6)	10	(6)	
Country of birth					0.44
United States	137	(84)	130	(81)	
Outside United States	26	(16)	31	(19)	
Education					0.48
High school or less	22	(14)	15	(9)	
Some college	114	(70)	116	(72)	
College or above	27	(17)	30	(19)	
Income					0.52
under $20,000	44	(27)	52	(32)	
$20,000-49,999	62	(38)	59	(37)	
$50,000-99,999	32	(20)	33	(21)	
$100,000 or above	25	(15)	17	(11)	
Employment status					0.95
Not employed	41	(25)	40	(25)	
Employed	122	(75)	121	(75)	
HIV Test History & Medical					
Last HIV test					0.57
Less than 1 year	150	(92)	148	(92)	
Over 1 year ago or never	13	(8)	13	(8)	
Has regular health provider	105	(64)	98	(61)	0.51
Insurance					0.57
No Insurance	52	(32)	52	(32)	
Private Insurance	91	(56)	83	(52)	
Public Insurance	20	(12)	26	(16)	

§ Wilcoxon ranksum test statistic for age; Chi-square test statistic for categorical variables

Table 6. Effects of the adapted Personalized Cognitive Counseling (PCC) intervention on various classes of substances and substance use concurrent with sexual risk among episodic substance-using MSM, Project ECHO, San Francisco, CA, 2010-2012

Substance Use Outcomes		Baseline[α] (%)	3 Month (%)	6 Month (%)	GEE Poisson Regression Models‡ RR	95% CI	P-Value
Any Substance Use (exclusive of alcohol)	PCC	85%	79%	83%	0.98	0.9-1.07	0.31
	Control	84%	82%	83%			
Any Alcohol	PCC	96%	94%	91%	0.93	0.89-0.97	<0.001*
	Control	98%	97%	99%			
Any Ecstasy	PCC	21%	24%	28%	1.31	0.94-1.83	0.12
	Control	24%	23%	22%			
Any GHB	PCC	7%	7%	7%	0.62	0.31-1.24	0.18
	Control	8%	7%	12%			
Any Marijuana	PCC	63%	62%	56%	0.84	0.73-0.98	0.02*
	Control	61%	66%	65%			
Any Methamphetamine	PCC	9%	9%	5%	0.72	0.36-1.42	0.34
	Control	10%	10%	8%			
Any Poppers	PCC	44%	30%	29%	1.04	0.74-1.46	0.82
	Control	41%	28%	26%			
Any Crack	PCC	2%	3%	4%	1.64	0.65-4.15	0.29
	Control	4%	4%	3%			
Any Cocaine	PCC	30%	26%	29%	1.05	0.77-1.43	0.76
	Control	35%	24%	30%			
Any Prescription Drugs	PCC	12%	10%	9%	0.57	0.31-1.03	0.06
	Control	11%	9%	15%			
Any Erectile Dysfunction Drugs	PCC	22%	16%	13%	0.51	0.33-0.79	<0.001*
	Control	16%	18%	21%			
Any UAI with Alcohol, Methamphetamine, Cocaine or Poppers	PCC	79%	34%	31%	0.85	0.61-1.17	0.25
	Control	74%	41%	33%			
		Baseline[α] (mean)	3 Month (mean)	6 Month (mean)	GEE Negative Binomial Regression Models‡ RR	95% CI	P-Value
No. UAI Events w/ Alcohol	PCC	2.28	0.83	0.75	0.69	0.39-1.2	0.19
	Control	2.26	1.13	1.01			
No. UAI events w/ Methamphetamine	PCC	0.17	0.09	0.087	0.26	0.08-0.84	0.02*
	Control	0.26	0.37	0.37			
No. UAI events w/ Cocaine	PCC	0.26	0.16	0.14	1.07	0.35-3.27	0.9
	Control	0.33	0.12	0.15			
No UAI events w/ Poppers	PCC	0.86	0.27	0.22	0.6	0.24-1.52	0.28
	Control	0.69	0.41	0.28			
No. binge drinking days (5+ drinks)	PCC	8.98	7.55	7.53	0.87	0.64-1.19	0.39
	Control	8.69	7.78	8.51			

Ordered Logistic Regression Models[α†]			
Outcome❖	**Odds Ratio**	**95%CI**	**P-value**
Alcohol intoxication frequency	0.54	0.34-0.85	0.007*
Methamphetamine use frequency	0.61	0.25-1.52	0.29
Cocaine use frequency	0.89	0.55-1.46	0.65
Poppers use frequency	1.05	0.63-1.73	0.85
SDS Alcohol	0.92	0.59-1.42	0.70
SDS Methamphetamine	0.79	0.27-2.32	0.67
SDS Cocaine	0.80	0.40-1.60	0.53
SDS Poppers	0.34	0.09-1.27	0.11

Notes: RR indicates rate ratio (i.e. the ratio of the intervention and control rates of change in the mean value of the outcome over time, our summary measure of the intervention effect. The linearity assumption was checked); CI, confidence interval; UAI, unprotected anal intercourse; SDS, severity of dependence scale score.[α] No significant differences in substance use outcomes were observed between PCC and Control conditions at baseline. †no evidence of violation from proportional odds assumption in all models. ❖ alcohol was measured as frequency of being intoxicated (i.e. "drunk or buzzed from alcohol); categories for alcohol and substance use are based no-use and frequency of use recoded into tertiles (i.e. 1-33 percentile, 34-66 percentile, 67-100 percentile); categories for severity of dependence scale are based on score of 0 and scores above zero recoded into tertiles.

Figure 1. Flow diagram of participant enrollment, allocation, and retention in Project ECHO by arm, San Francisco 2010-2012

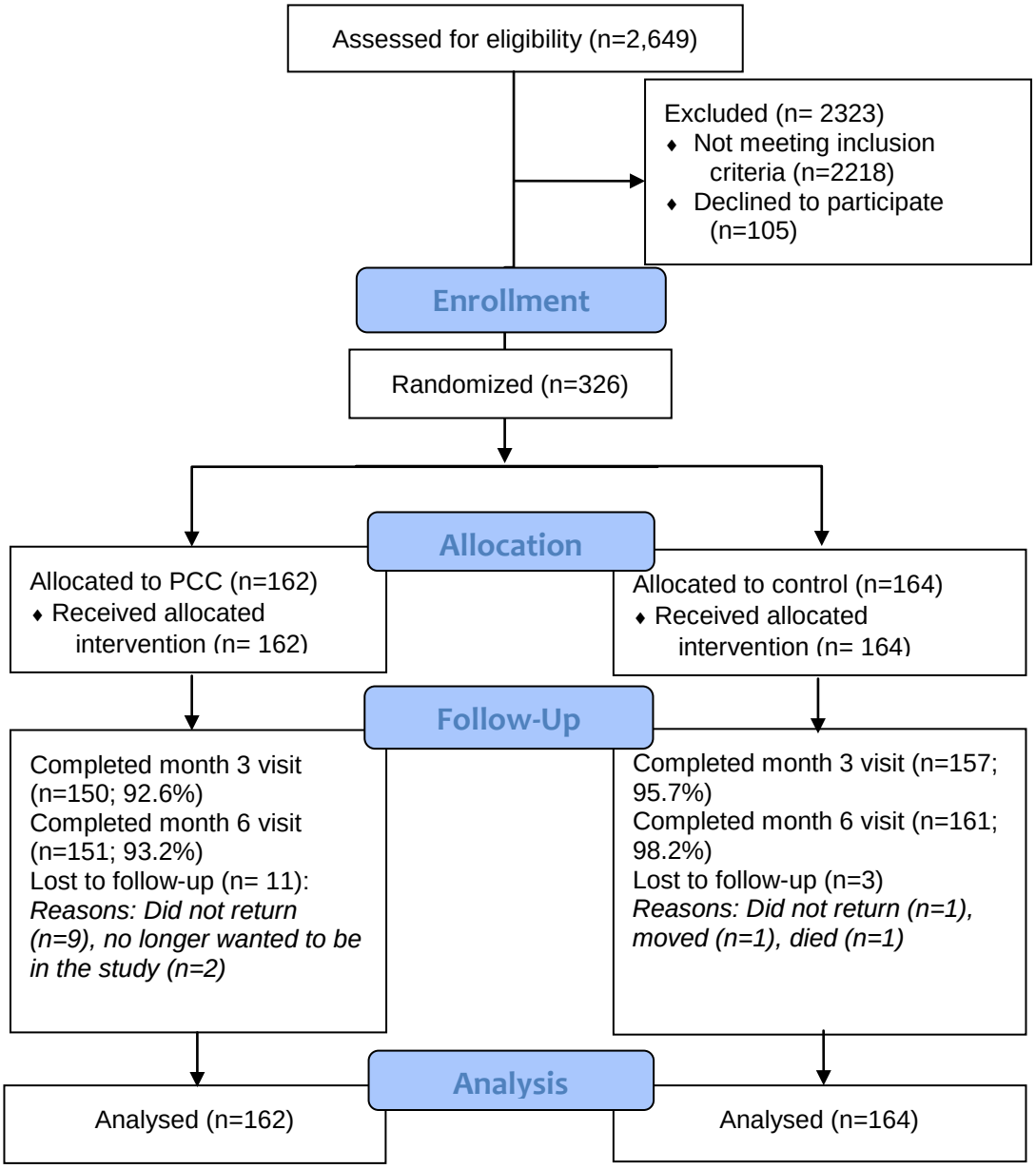
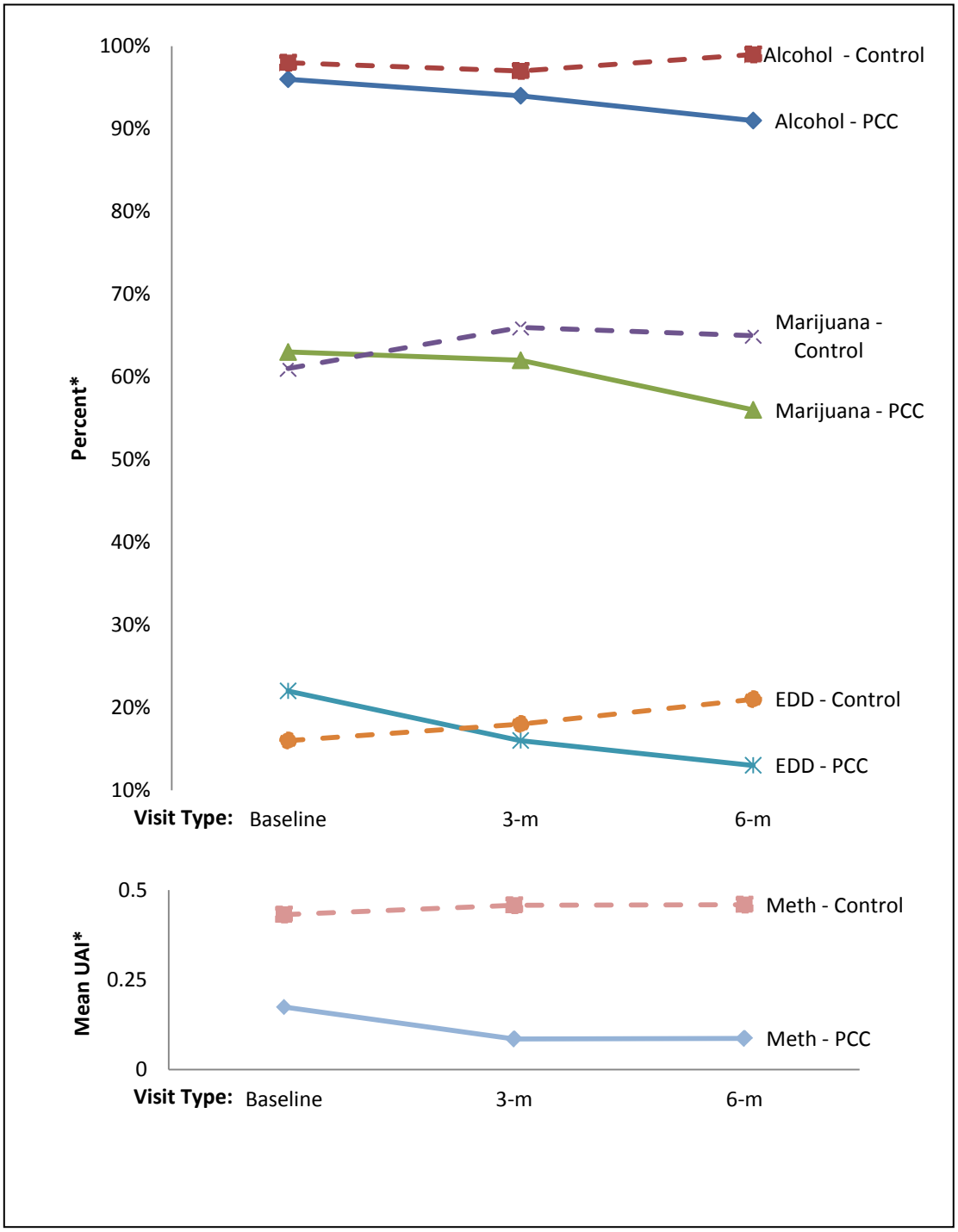


Figure 2. Substance Use Outcomes in Project ECHO Study, by arm - San Francisco, 2010-2012



Chapter 3: Self-reported alcohol abstinence associated with ART initiation among HIV-infected persons in rural Uganda

Introduction

In 2010, five and a half percent of the total burden of disease around the world has been attributed to alcohol consumption, which is also causally related to more than 60 chronic and acute health conditions [1, 2]. Heavy alcohol use, in particular, has been associated with a wide range of societal, economic, and medical consequences [2-4].

Hazardous alcohol consumption is highly prevalent in sub-Saharan Africa (SSA) [5]. Per-capita, Uganda has among the highest alcohol consumption in the world [5]. One study in primary care clinics in Kampala, Uganda observed a 17% and 10% prevalence of hazardous alcohol consumption and alcohol dependence, respectively [6]. Despite the high prevalence of heavy alcohol use in SSA and in Uganda, interventions to reduce alcohol use are not widespread in this region, particularly outside large urban areas, underscoring a major public health gap [7]. Although provision of health education materials and cognitive behavioral therapy may be promising in reducing alcohol consumption among HIV-infected individuals in some settings, scale-up of these programs remain limited[8-10]. Moreover, problem alcohol use is believed to often go undetected in this region; one study in primary care settings found that only 7% of drinkers have been asked about their alcohol consumption by their medical providers [6].

Alcohol use has been associated with increased risk of HIV acquisition and transmission in SSA [11-17]. There is compelling data linking alcohol consumption and increased sexual risk behaviors—and consequently secondary HIV transmission—in SSA [18]. In addition, alcohol consumption has been associated with delays in detection of HIV-infection, poor HIV health outcomes and sub-optimal HIV care [7, 19, 20]. Drinking may also play a role in receipt of antiretroviral therapy (ART) and alcohol intoxication may also affect ART efficacy through poor

adherence or potential changes in metabolism of ART [20-23]. Some, though not all, studies have found independent associations between alcohol consumption and HIV disease progression [7, 22].

However, little is known about the patterns of alcohol use among HIV-infected individuals in SSA. There is also very limited data on the impact of ART initiation on alcohol consumption. One study in Kampala, Uganda, found that ART initiation was associated with a 50% increase in odds of reporting abstinence from alcohol for at least six months among those with HIV [24]. Given the interplay between HIV and alcohol use, it is important to characterize the extent of alcohol consumption, particularly among HIV-infected individuals, in this region. Moreover, identifying HIV-infected persons who do not become abstinent from alcohol can assist with targeting and development of effective interventions for others to reduce harms associated with alcohol [7]. We therefore sought to evaluate alcohol consumption patterns and prospective predictors of self-reported initiation of abstinence from drinking among HIV-infected individuals initiating ART in Mbarara, Uganda.

Methods

Participants and Study Design

Data from this analysis was collected as part of the Uganda AIDS Rural Treatment Outcomes (UARTO) study, a prospective cohort of HIV-infected individuals initiating ART. Participants were eligible for enrollment in this cohort if they were HIV-infected, ART-naïve, at least 18 years of age and lived within 60 kilometers from the Mbarara Regional Referral Hospital Immune Suppression Syndrome (ISS) Clinic in Mbarara, Uganda. A representative from the study recruited and screened individuals obtaining antiretroviral medication for the first time from the ISS pharmacy for eligibility. All eligible patients who consented to participate were enrolled

in the cohort until the target sample size for the study was reached. In quarterly visits, biological specimens were collected, and participants were interviewed face-to-face with standardized questionnaires administered in English or Runyankole by native speakers.

Measurements

Data on sociodemographic characteristics and quality of life measures, including mental health summary (MHS) and physical health summary (PHS) were collected in interviewer-administered structured questionnaires. MHS and PHS are two of the domains from the Medical Outcomes Study HIV Survey (MOS-HIV)—a measure of health function that has been previously validated in Uganda [25] and has been associated with AIDS-related events [26]. MHS and PHS scores range between 0-100, with higher scores corresponding with better function and quality of life. Self-reported alcohol consumption, including frequency and volume was elicited quarterly. At baseline, the World Health Organization's 10-item Alcohol Use Disorder Identification Test (AUDIT) was administered to assess alcohol consumption from the past 12 months (range:0-40) [27]. Hazardous alcohol consumption cut-offs for men and women were scores of eight and five, respectively. These cut-offs were observed to have the most optimal sensitivity and specificity for hazardous drinking among men and women in a population-based study in Finland [28]. Blood draws were also conducted at quarterly visits for CD4+ T-cell counts. The procedures for this study were approved by the Committee in Human Research at the University of California at San Francisco, Partners HealthCare, Mbarara University of Science and Technology and the Uganda National Council on Science and Technology.

Statistical Analysis

At baseline, we estimated the proportion of current alcohol drinkers (i.e. those who reported alcohol consumption within the prior 3 months), former alcohol drinkers (i.e. those who

reported alcohol consumption over 3 months ago), and lifetime abstainers of alcohol. Among current drinkers at baseline, we fitted a pooled logistic regression (PLR) model to evaluate predictors of time to first becoming abstinent from alcohol for at least 90 days using a complete case analysis. Because the majority of participants reported becoming abstinent at month 3 or 6 visits, time intervals were categorized into 3 groups: 1) month 3 visits (referent), 2) months 6 visits, and 3) months 9 visits or later. PLR is appropriate for outcomes that are interval-censored between visits; furthermore, with the inclusion of the categorical variable for interval in the model, PLR provides estimates of the between-interval differences in the incidence rate for abstinence. We evaluated the relationship between abstaining from drinking and the following: age, sex, education, religion, literacy, and baseline AUDIT score (evaluated as a continuous measure and dichotomized as hazardous vs. non-hazardous). Time-varying predictors of interest were time since ART initiation/baseline visit, MHS score, PHS score, and CD4 cell count. For model-building, we used the algorithm suggested by Hosmer and Lemeshow in which predictors that were statistically significant in the bivariate-level using a p-value cut-off point of 0.25 were included in the larger multivariable model [29]. The final multivariable model was arrived at using a step-wise backward procedure; likelihood ratio tests were used to confirm that nested-models fit the data as well as larger models. At year one and two of follow-up, 2% and 5% of UARTO participants were lost to follow-up, respectively. Moreover, 12% of data on alcohol consumption were missing due to missed visits. We therefore conducted multiple imputation using iterative chained equations with STATA 12.1 (College Station, TX) to examine our findings' sensitivity to missing data. For multiple imputation, missing continuous follow-up data on MHS, PHS, and CD4 count were imputed using predictive mean matching while missing binary data on alcohol consumption was imputed using logistic regression; 10 datasets were imputed using demographic (e.g. education, literacy, religion, gender, age) characteristics, AUDIT score, PHS score, MHS score, and CD4 cell count. The 10 imputed datasets were analyzed using STATA mi estimate, which combines dataset-specific results to estimate

standard errors, confidence intervals, and p-values that reflect the imputation of missing data via established methods [30].

Results

Sample Characteristics

Among the 502 HIV-infected participants enrolled in the UARTO cohort from June 2005 to May 2011, 108 (21.5%) were current drinkers, 206 (41.0%) were former drinkers, and 188 (37.5%) were lifetime abstainers of alcohol (**Figure 3**). The median number of days between baseline alcohol assessment and ART initiation was 1 day (inter-quartile range: 0-2); 96% of participants initiated ART within 15 days of baseline alcohol assessment. Of the current drinkers at baseline, over half were male (51.9%), most were literate (78.7%), and most only had primary education or lower (63.9%) (see **Table 7**). Among current drinkers, 67 (62.0%) were considered hazardous drinker at baseline by past-year AUDIT score (median 9; IQR: 5-15). The median number of drinking days among current drinkers was 3.5 (IQR: 1-10) and the majority reported drinking less than 5 drinks on a typical drinking day (68.5% had 1 or 2 drinks, 17.6% had 3 or 4). Many have felt guilty about their drinking (37.0%) or the need to cut down on their alcohol consumption (49.1%).

Longitudinal Analysis

Analyses of becoming abstinent from alcohol were restricted to 108 current drinkers at baseline, who contributed 167.75 person-years of follow-up, with a median follow-up time of 3.6 median years of follow-up [IQR: 2-4.8]. Among the current drinkers, 90 (83.3%) reported first abstaining from alcohol for at least 90 days during follow-up. As illustrated in **Figure 4**, the majority (n=50) of those who abstained reported doing so during the first 90 days after ART initiation—that is by their 3-month visit. Becoming abstinent was less common later during

follow-up; 14 participants became abstinent by 6-month visit and the 26 participants became abstinent by 9-month visit or later. Among the 90 who abstained from alcohol for at least 90 days, 69 participants (76.7%) reported remaining abstinent, while 21 (23.3%) resumed drinking at some point during the course of the 6-year follow-up (4 relapsed at 6 month, 2 at 9 month, and 15 after 9 month). For those who remained abstinent, the median duration of follow up was 3.25 years (IQR = 1.6-4.5).

Multivariable Pooled Logistic Regression

Becoming abstinent from alcohol for at least 90 days was independently associated with lower AUDIT score at baseline (AOR 0.95 (95% CI 0.91-0.99)), lower PHS score at baseline (AOR 0.92 (95% CI 0.87-0.97)), and decreases in PHS score at follow-up visits (AOR 0.92 (95% CI 0.88-0.97)), while controlling for changes in CD4 count during follow-up in multivariable analysis. Participants were also most likely to report alcohol abstinence in the first 90 days immediately after ART initiation (the 3 month visit); becoming abstinent from alcohol was less likely at later visits for those who continue to drink. Participants were most likely to abstain from alcohol during the first three months after ART initiation; among those still at drinking, the odds of abstaining from alcohol by 6 month visits and after 9 months were 0.25 (95% CI 0.10-0.61) and 0.04 (95% CI 0.02-0.09), respectively, compared to the odds of abstaining at month 3. The findings were similar in PLR analysis which used multiple-imputation (**Table 7**).

Discussion

Among HIV-infected individuals in Uganda, the prevalence of current alcohol use was modest but a high proportion of current drinkers reported drinking at hazardous levels the year prior to ART initiation. This finding is broadly consistent with the high rates of hazardous alcohol consumption among drinkers previously observed in other Ugandan samples overall, and

among HIV infected individuals [6, 19, 24]. Most significantly, a very large proportion of current drinkers at baseline reported becoming abstinent from alcohol for at least 90 days immediately after initiating ART, and most of those remained abstinent, findings which have not previously been reported.

We found that those with higher AUDIT scores at baseline were more likely to persist in drinking alcohol during follow-up. A three-question alcohol screen at clinic entry using the AUDIT-C, comprised of the first three consumption questions of the AUDIT, is standard procedure in this clinic [31]. This suggests that further measures to address heavy alcohol consumption may be warranted. In addition, implementing screening for problematic or hazardous alcohol consumption in HIV-treatment clinics where it is not yet standard is vital, since identifying those with alcohol abuse or dependence is the first step toward referrals to/provision of effective treatment [32]. Moreover, efforts to develop focused on interventions for hazardous drinkers who continue to drink should be prioritized.

We also observed that individuals with greater improvement in physical function as measured by PHS were less likely to report becoming abstinent from alcohol. It is possible that as perceived physical health improved, participants may have perceived that alcohol no longer posed harm to their health, and consequently continued drinking. Similarly, those who had greater physical health scores at baseline were also less likely to report abstinence from alcohol. It is possible that compared to those with poor physical function, those who had better physical health may not have felt a compelling reason to abstain from alcohol. Conversely, participants with poor physical health may have also abstained from alcohol because they were too ill to drink. This finding is important because ART is increasingly being initiated prior to the onset of symptoms, which suggests that more people may be drinking alcohol while on ART, therefore raising concerns about the effect of alcohol on early ART adherence.

In addition, we observed that among those still at risk, a high proportion of current alcohol drinkers reported abstaining from alcohol immediately after ART initiation. These findings are consistent with another Ugandan study which found that self-reported abstinence from alcohol was associated with ART initiation among HIV-infected individuals [24]. Of note, as drinking continued beyond the first quarterly visit after ART initiation, the likelihood of becoming abstinent from alcohol had decreased dramatically. The reductions in alcohol consumption were concurrent with ART initiation. Those who continued to drink more than three months after they initiated ART were unlikely to ever quit on their own. Interestingly, these reductions in alcohol consumption after ART initiation are mirrored by other health improvements in this same cohort—in UARTO, ART initiation has been associated with increased food security and reductions in depression [33, 34]. It is possible that initiating ART provides a range of collateral health benefits. Interestingly, these reductions in alcohol consumption after ART initiation are mirrored by other health improvements in this same cohort—in UARTO, ART initiation has been associated with increased food security and reductions in depression [34, 35]. It is possible that initiating ART provides a range of collateral benefits that are similar to engaging in primary care. Indeed, a prospective study of individuals in a drug/alcohol detoxification unit found that receipt of primary medical care was associated with significant declines in alcohol consumption and severity of use [36] and a similar effect for substance abuse has also been shown [37]. It is possible that engagement in health care and/or discussions about health preserving behaviors have some effect. While motivation to change behavior is the foundation of many brief interventions, many which have been successful, especially in primary care [38], additional studies are needed to understand why those initiating ART reduce their alcohol consumption.

The mechanism behind our findings on alcohol abstinence during follow-up is not completely clear. Two recent randomized controlled trials, one among hospital outpatients [10]

and one among primary care patients with active tuberculosis [9], compared brief motivational interventions to providing health education information on alcohol consumption. Both studies found equivalent reductions in drinking between both conditions [9, 10]. This suggests that in some settings minimal intervention may be all that is needed; thus information about the effects of alcohol on HIV disease and ART adherence may be sufficient. Counseling to promote ART adherence is conducted by the ISS clinic, and alcohol consumption is sometimes addressed, which may have a positive effect on drinking. At this time, there is no standard protocol in the clinic for patients who drink alcohol. Instead, staff are encouraged to communicate about reduction of alcohol after assessing the levels of consumption, however the delivery of this message may vary widely between staff (Personal Communication: Muyindike, 2013).

Another plausible explanation for declines in drinking is assessment reactivity. Alcohol researchers have previously recognized that participants react to study protocols involving collection of data on alcohol use; more frequent and more comprehensive alcohol assessments have been associated with declines in alcohol consumption and better drinking outcomes [39-42]. Researchers posit that the assessment of drinking behavior in itself can lead to reductions in alcohol consumption [39, 42]. In this study, participants were interviewed about their drinking behaviors on a quarterly basis, and research assistants may often be perceived as health care workers. Although study participants were not receiving a formal alcohol intervention, it is likely that at least some individuals were reactive to these assessments and changed their drinking behavior as a result of these regular interviews.

Alternately, participants may also fear that alcohol consumption could be used as an exclusionary criterion from ART receipt and therefore under-report their current alcohol consumption; indeed, health providers have delayed provision of ART among alcohol drinkers due to treatment adherence concerns [43, 44]. Some of these data were collected during the

early stages of large-scale ART roll out, and the perception that ART was being rationed is plausible during the earlier periods of the study. Social desirability bias may also provide at least a partial explanation for our findings [24]. A recent nested-study within UARTO (n=61) observed a two-fold increase in self-reported alcohol consumption when alcohol biomarkers were collected concurrently during alcohol assessment confirm that at least some participants are under-reporting alcohol consumption [45]. Unfortunately, because we did not systematically collect whole blood samples to test for alcohol biomarkers such as phosphatidylethanol (PEth), the extent of under-reporting is unclear across the entire sample. Future studies among HIV-infected individuals should collect specimens for biomarkers of alcohol consumption when possible as they function as complementary objective measures of alcohol use and potentially improve the accuracy of self-reported consumption [45-47]. Qualitative studies currently underway (JH) may also help determine whether reported reductions in alcohol consumption at this clinic are due to assessment reactivity, the influence of counseling by the staff, concern about the effects of alcohol on ART efficacy, or otherwise. However, because many of our results were consistent with previous findings and decreased levels of becoming abstinent among more hazardous drinkers and those reporting better health [24], we feel that at least some of the decline in drinking is real.

This study has several limitations. First, the modest number of current drinkers in our sample at time of ART initiation may have reduced our power to detect statistically significant associations and precluded us from evaluating other less common alcohol drinking patterns in the study, such as abstaining and then relapsing to drinking. This may explain the lack of association we observed for other characteristics previously shown to be associated with alcohol abstinence, such as gender and CD4 cell count [24, 48]. However, although we did not observe gender differences for alcohol abstinence among current drinkers, we note that at baseline, women were much less likely to be current drinkers compared to men (14.3% vs.

37.1%), suggesting that women may be more likely to never start drinking and to quit earlier, consistent with the literature. Additionally, the majority of those initiating ART in this study were immunologically quite compromised (i.e. had low CD4 cell count) and this low variance in CD4 cell count at baseline may explain the lack of association with quitting alcohol. Physical health score, which was inversely related to quitting, was a better predictor in this study. Thus, it would be important to replicate this analysis and also explore predictors of stopping and resuming drinking with a larger sample that has greater prevalence of alcohol consumption.

As previously described, the self-reported data used for alcohol consumption are subject to recall and/or social desirability and other reporting biases. Similar to other non-randomized studies, we cannot rule out the possibility of unmeasured confounders in our analysis of correlates of becoming abstinence. Moreover, this study is limited to a sample of HIV-infected individuals who are ART-naïve from a single HIV-treatment clinic. Thus, the findings may not necessarily be generalizable to other populations or settings. An additional limitation is that the time-dependent covariates CD4 count and change in MHS and PHS scores may in part mediate the effect of visit interval, thus understating its importance. Despite these limitations, the findings on self-reported abstinence were consistent between the complete case pooled logistic regression models and multiple imputation sensitivity analyses for missing data, suggesting that these results are robust. In addition, our analytic findings were consistent with the findings of other studies.

These data underscore the need to implement screening tools to increase detection of problematic alcohol consumption in HIV care settings, and intervention approaches [49]. The findings on the inverse relationship between physical health and alcohol consumption has important implications as countries in SSA begin to implement treatment guidelines that call for earlier initiation of ART. If ART occurs prior to the onset of HIV-related symptoms, alcohol

consumption during treatment may become more common, and HIV providers should be aware that more of their patients may be drinking alcohol. Hazardous alcohol use may influence the efficacy of ART through behavioral and biologic pathways and function as a barrier to optimal HIV-care [7, 20, 21].

Moreover, our study provides insight on the longitudinal alcohol consumption patterns of HIV-infected adults initiating ART and the baseline prevalence of alcohol use in this population. These findings can inform the development of new alcohol interventions in SSA, where hazardous alcohol consumption is common and additional evidence-based interventions outside large urban areas are needed. These data can also inform the targeting and translation of screening and brief interventions for harmful alcohol use—which have been tested in hospital settings, patients with tuberculosis in primary care settings, and in university students in SSA—for HIV-infected individuals [9, 10, 50]. Moreover, these results can also facilitate the identification of drinkers who are initiating ART whom may benefit from intensive behavioral interventions, such as cognitive behavioral therapy—which showed promising results in reducing alcohol consumption among HIV-infected patients in Kenya [8]. Ideally, these existing evidence-based interventions should be made available to sub-groups who have difficulty abstaining from alcohol, particularly those who have more hazardous alcohol consumption prior to ART initiation and those with good physical health who may not necessarily feel an urgency to reduce their consumption. The data also suggest that ART initiation may be an opportune time to implement additional harm reduction interventions for alcohol consumption. As many patients appear to attempt abstaining from alcohol during this period, many individuals may benefit from additional counseling to reduce relapse or resumption of hazardous drinking.

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Table 7. Baseline Characteristics of HIV-Infected Current Alcohol Drinkers, Former Drinkers, and Never Drinkers initiating ART in Rural Uganda

	Never Drinkers (Lifetime Alcohol Abstainers, N=188)		Former Drinkers (Alcohol >90 days of baseline, N=206)		Current Drinkers (Alcohol within 90 days of baseline, N=108)	
	N median	(row %) (IQR)	N median	(row %) (IQR)	N median	(row %) (IQR)
Demographics						
Age, median (IQR)	33.5	(27-39)	35	(30-40)	35	(30-39)
Gender						
Female	152	(44.4)	141	(41.2)	49	(14.3)
Male	34	(22.5)	61	(40.4)	56	(37.1)
Education						
Primary or Less	137	(40.1)	136	(39.8)	69	(20.2)
Beyond Primary	45	(36.9)	48	(39.3)	29	(23.8)
Literacy						
Illiterate	38	(37.6)	43	(42.6)	20	(19.8)
Partial or Fully Literate	145	(37.3)	159	(40.9)	85	(21.9)
Religion						
Protestant	97	(39.0)	102	(41.0)	50	(20.1)
Catholic	46	(26.6)	76	(43.9)	51	(29.5)
Moslem	29	(70.7)	9	(22.0)	3	(7.3)
Other	14	(46.7)	15	(50.0)	1	(3.3)
Clinical						
CD4 Count, median (IQR)	131.5	(76-201)	134	(67-192)	124	(73.5-217.5)
Mental Health Score (MOS), median (IQR) †	52.3	(44.4-56.6)	51.0	(44.2-56.8)	53.1	(47.1-59.4)
Physical Health Score (MOS), median (IQR) †	53.3	(42.4-58.6)	52.2	(42.0-57.1)	55.6	(47.0-59.8)

Baseline Alcohol Consumption among Current Alcohol Drinkers	**N median**	**[column %] (IQR)**
Drinking days in past 30 days, median (IQR)	3.5	(1-10)
Alcohol Use Disorders Identification Test (AUDIT) Score – in the past year, median (IQR)	9	(5-15)
Hazardous Alcohol Consumption by AUDIT Score	67	[62%]
Drinks on a typical day when you were drinking in the past year		
1 or 2 drinks	74	[68.5]
3 or 4 drinks	19	[17.6]
5 or more drinks	10	[9.3]
"cannot estimate"§	4	[3.7]
Heavy episodic drinking (having six or more drinks on one occasion) in the past year		
Never	71	[65.7]
Less than monthly	6	[5.6]
Monthly	10	[9.3]
Weekly	7	[6.5]
Daily/mostly daily	5	[4.6]
"cannot estimate"§	8	[7.4]
Ever hospitalized due to drinking	3	[2.8]
Ever attended a 12-step program	1	[1.0]
Ever felt they should cut down on drinking	53	[49.1]
Ever felt guilty about drinking	40	[37.0]

Notes: Percent may not add up to 100 due to rounding. †Measures from Medical Outcomes Study (MOS) health-related quality of life measures in HIV/AIDS; higher scores correspond with better physical or mental health function. §Participants who reported that they "cannot estimate because of use of non standardized non-bottled home-brewed beverages."

Table 8. Pooled Logistic Regression Model for Becoming Abstinent from Alcohol for at least 90 days among HIV-Infected Alcohol Drinkers initiating ART in Rural Uganda

	Complete Case		Multiple Imputation	
	Adjusted OR* (95% CI)	**P-value**	**Adjusted OR* (95% CI)**	**P-value**
Visit Interval				
Month 3 visit	1.00		1.00	
Month 6 visit	0.25 (0.10-0.61)	0.002	0.32 (0.13-0.81)	0.016
Month 9 visit or later	0.04 (0.02-0.09)	<0.001	0.05 (0.02-0.09)	<0.001
Baseline AUDIT Score (past 12 months)[2]	0.95 (0.91-0.99)	0.049	0.95 (0.91-0.99)	0.042
Baseline Physical Health Score	0.92 (0.87-0.97)	0.001	0.92 (0.87-0.97)	0.002
Change in Physical Health Score at Follow-up	0.92 (0.88-0.97)	0.001	0.92 (0.88-0.97)	0.001

Note: *Data only shown for statistically significant findings, models also adjusted for changes in CD4 count at follow-up

Figure 3. Alcohol consumption in UARTO Cohort during Baseline and Follow-Up Visits

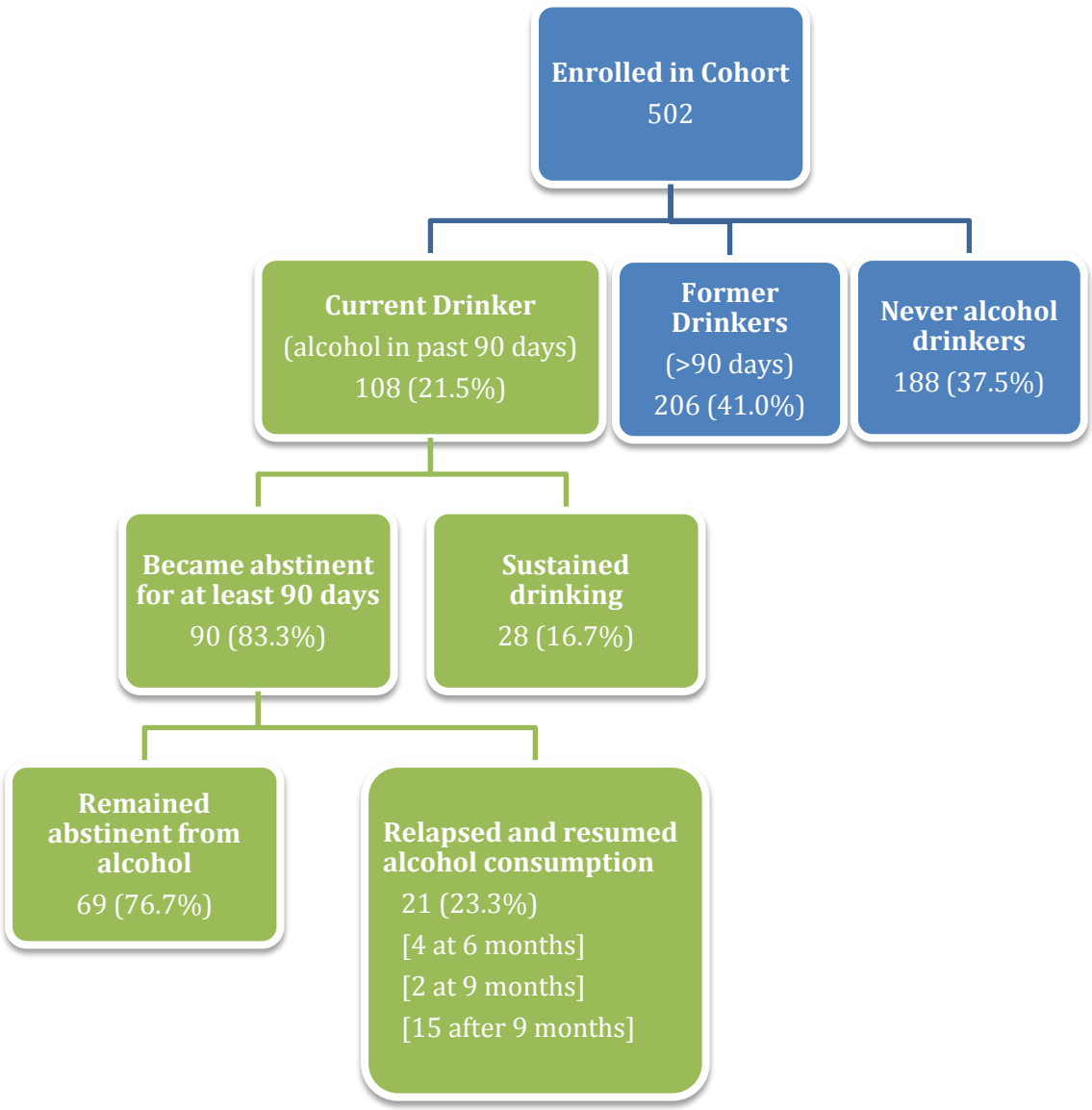
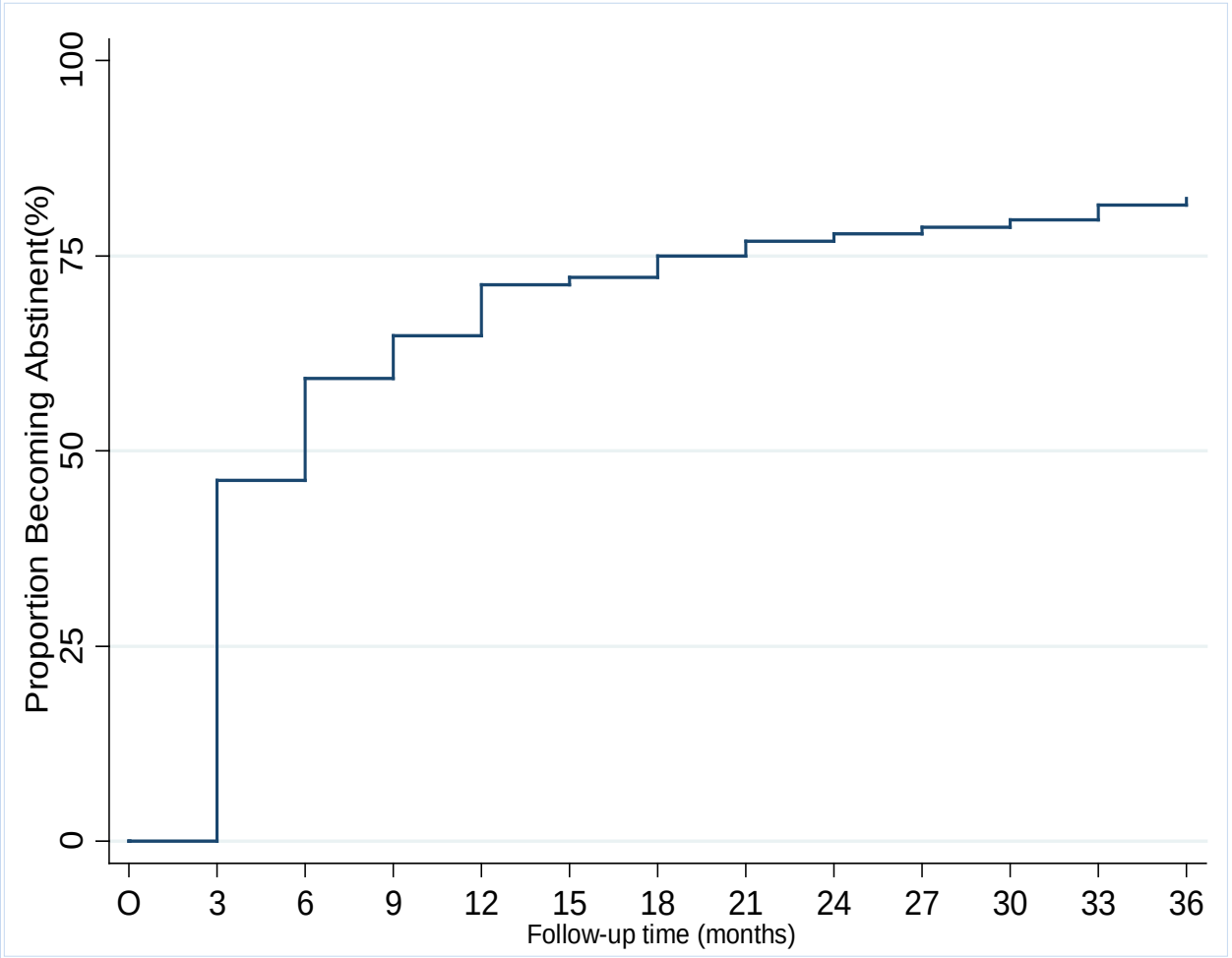


Figure 4. Time to first becoming abstinent from alcohol for 90 days among 108 baseline current drinkers in UARTO Cohort



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