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Alcohol use patterns and subsequent sexual behaviors among women, men who have sex with men and men who have sex with women engaged in routine HIV care in the United States

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Institutional review boards at each CNICS site approved the collection and analysis of the clinical data.

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INTRODUCTION

Alcohol misuse is common among people living with HIV (PLWH) with estimates among PLWH in care ranging from 8% to 27% (1,2) compared with 7% estimated in the US general population (3). Across the HIV care continuum, alcohol misuse is associated with increased HIV incidence (4,5), HIV prevalence (2), worse antiretroviral adherence (6,7) worse retention in care (8), adverse clinical outcomes, including lack of viral suppression (8), and increased mortality (9,10). It is also associated with sexual behaviors that can increase risk of HIV transmission including vaginal and anal sex; multiple sex partners; condomless sex; and sex under the influence of alcohol or drugs (11–13). Alcohol appears to influence sexual behaviors through a variety of mechanisms by increasing sexual arousal, sexual disinhibition, myopia for appreciation of consequences, and expectancies about the effect of alcohol on sexual interest and behaviors (14–16). Despite current availability of pre-exposure prophylaxis, behavioral interventions are still a mainstay of HIV prevention and intervention to reduce HIV transmission behaviors and to reduce the effects of contributing factors such as alcohol misuse.

Systematic reviews have established the association between alcohol use, particularly binge drinking (≥4/≥5 drinks/occasion for women/men), and sexual behaviors among PLWH (17–19). Most of the studies combined outcomes for women and men, report on men, or report on men who have sex with men (MSM). Across these studies, the specific influence of alcohol on sexual behaviors varied depending on how alcohol consumption was measured, the sexual behaviors examined, and the gender and sex of PLWH and their partners (19). HIV studies separately examining women, MSM, and men who have sex with women (MSW) provide relevant information about the associations between alcohol use and sexual behaviors. Where gender or sex differences are of interest, studies that include multiple groups provide the opportunity to compare differences that may be a function of gender or sex rather than a function of the particular sample or setting characteristics.

For example, in the few HIV studies that have jointly examined women, MSM, and MSW, women had a lower prevalence of alcohol use, but a higher prevalence of both alcohol use before sex and condomless intercourse (13,19,20). Women who reported binge drinking (vs no binge drinking or no drinking) were more likely to be sexually active, have had multiple sexual partners, and have engaged in anal or condomless sex; MSM and MSW did not as consistently show such associations between binge drinking and sexual behaviors (11,20,21). However, not all studies have observed a higher prevalence of sexual behaviors under the influence of alcohol among women compared with men (22). In comparisons of MSM and MSW, MSM have had a higher prevalence of alcohol use, particularly binge use, and increased likelihood of sexual activity, multiple sex partners, and condomless intercourse (22,23). Information about how specific patterns of alcohol use affect particular sexual behaviors among women, MSM and MSW can guide more tailored secondary prevention efforts.

Additionally, most studies examining alcohol and sex behaviors among PLWH that have stratified by sex or gender and partner's sex have been cross-sectional and thus inferences about temporal primacy and causality are limited (24). Event level and longitudinal studies that could more effectively examine potential causality have tended to focus on MSM (25–29) and to a lesser extent on combined samples of PLWH (30,31); relatively less is known about women. To effectively prevent and reduce HIV sexual transmission behaviors, the evidence base should include longitudinal studies that can refine and adapt theoretical frameworks and behavioral interventions (24).

Finally, drug use is associated with sexual behaviors and the type of behavior can vary according to the substance used (32,33). Given the substantial overlap between alcohol and recreational drug use among PLWH (20), understanding their interaction and effect on subsequent behaviors is important for designing alcohol and drug use interventions.

In this study, we examined the association between quantity and frequency of alcohol use and subsequent sexual behaviors across a large, geographically diverse United States (US) cohort of PLWH enrolled in continuity HIV care and participating in the Centers for AIDS Research Network of Integrated Systems (CNICS). Because of the cohort's size, we had the opportunity to examine women, MSM, and MSW separately. We also investigated interactions between alcohol and specific recreational drug use (cocaine/crack, methamphetamine and marijuana) on risk of subsequent sex behaviors. Based on our own work and that of others (11,13,21,23,), we hypothesized that binge drinking would be strongly associated with sexual transmission behaviors in women and MSM but weakly associated with sexual transmission behaviors in MSW.

METHODS

Study Sample

CNICS is a cohort of PLWH receiving continuity HIV care at one of eight HIV clinics around the United States. Comprehensive clinical data from PLWH in CNICS gathered from electronic medical records and other data sources provide research infrastructure to support HIV clinical outcomes and comparative effectiveness research. Participating clinics are located at University of Alabama Birmingham, University of California San Francisco, University of Washington, University of California San Diego, Fenway Health/Harvard University, University of North Carolina Chapel Hill, and Johns Hopkins University. Briefly, CNICS participants self-report age, gender, race, ethnicity, and probable route of HIV acquisition upon enrollment into the clinic. HIV viral load and CD4 cell count are measured as part of routine clinical care, and results are extracted from laboratory databases. Participants consent to participate in and share their data with CNICS. Institutional review boards at each CNICS site approved the collection and analysis of routinely collected clinical data. Full details of the CNICS cohort are available elsewhere (34).

In addition to clinical data, patients at seven of the eight CNICS sites participate in patient reported outcome (PRO) assessments. (The 8th clinic, Case Western Reserve University, is a CNICS site but only recently initiated collecting PRO so data are not included.) PRO are collected approximately every 4–6 months in conjunction with a clinical visit (34,35).

Patients who are medically unstable, cognitively impaired, or intoxicated at the time of a clinical encounter, or who do not speak English, Spanish, or Amharic are not solicited to participate in PRO assessments. Tablet computers are used to complete the assessments that require approximately 10–12 minutes. PRO includes patients' self-reported recent depressive symptoms, alcohol use, recreational drug use, and sexual transmission behaviors. We included all CNICS participants in the current study who completed at least two PRO assessments between January 2011 and June 2014. We classified PLWH based on their reported sex and HIV acquisition risk factors at first CNICS visit into women, men who have sex with women exclusively (MSW) or men who have sex with men (MSM). The very low frequency of MSM having sex with women (< 6.0%) precluded separate categorization and thus further analysis. To ensure that self-reported alcohol and substance use (exposure) occurred before the self-reported sexual behaviors that we examined as our outcome, we analyzed person-periods defined by paired, proximate PRO assessments such that alcohol use was drawn from one assessment (the index assessment at time 1, prior 12 months) and sex behaviors drawn from the earliest subsequent assessment (time 2, prior 6 months). We required that the subsequent assessment had to be at least 3.5 months (≥135 days) after the index assessment. We used this time frame because it corresponded to the approximate period in which PLWH were returning to the clinic for their 4–6 month medical visit and next PRO.

Individual study participants could contribute multiple person-periods. For example, if a patient had three PRO assessments each separated by ≥135 days, they contributed two person-periods, where the first person-period considered alcohol use at time 1 and sex behavior at time 2, and the second person-period considered alcohol use at time 2 and sex behavior at time 3.

Exposure

Alcohol use over the prior year was measured with the 3-item Alcohol Use Disorder Identification Test (AUDIT-C) (36). The AUDIT-C questions ask about use in the prior 12 months including: 1) ''How often do you have a drink (wine, beer or liquor) containing alcohol?'' (Never; Monthly or less; 2 to 4 times a month; 2 to 3 times a week; 4 or 5 times a week or 6 or 7 times a week); 2) ''How many drinks containing alcohol do you have on a typical day when you are drinking?" (0 to 10 or more); and 3) "How often do you have 4 or more (women)/5 or more (men) drinks on one occasion?" (Never; less than monthly; monthly; weekly; daily or almost daily). At the start of the AUDIT-C, "alcoholic drink" was defined using pictures to exhibit types and amounts of alcohol contained in a "standard drink," e.g. a 8–9 ounces can of malt liquor or a glass containing 1.5 ounces of 80 proof distilled liquor. Hazardous drinking was defined as >7 drinks per week for women and >14 drinks per week for men, in accordance with NIAAA definitions. "Binge drinking" was defined as ≥4 drinks on one occasion for women and ≥5 drinks on one occasion for men also in accordance with NIAAA definitions. Based on respondents' answers at the beginning of a person-period, we classified person-periods into non-drinking; Moderate/non-binge; Moderate/binge; Hazardous/non-binge; or Hazardous/binge. Using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (37,38), patients answered separate questions about cocaine/crack, methamphetamine, illicit opioids or marijuana: "In the past 3

months, how often have you used [drug]?" (Never; once or twice, monthly, weekly, daily or almost daily).

Covariates

Patients reported their date of birth, race and ethnicity upon enrollment into medical care. We classified patients based on race and ethnicity as Hispanic, non-Hispanic white, non-Hispanic black, or non-Hispanic other race. We used year of birth and date of the index PRO to determine patients' age at the start of each person-period. PRO measured depressive symptoms in the prior 2 weeks using the Patient Health Questionnaire (PHQ)-2 (39). We classified person-periods as "depressed" if the PHQ-2 on the index PRO was ≥3. Laboratory values were assigned to a given person-period if they were collected up to 180 days in advance of, or 10 days after, the index PRO. We classified HIV viral load ≤100 copies/mL as undetectable to account for variability in laboratory threshold classifications. Some laboratory tests were conducted with a threshold for HIV RNA detection >50 copies/mL, thus using <50 copies/mL as the threshold for "undetectable" would have incorrectly classified some persons as "detectable." Also, as the threshold for sexual transmission is around 1500 copies/mL (40), and risk of sexual transmission was our interest, the use of a higher threshold to classify sex as 'unsafe' should not affect our inference.

Outcomes

Sexual behavior outcomes were based on responses to the PRO assessment closing a person-period. The questions included on the PRO asked about sex behaviors in the 6 months prior to the PRO assessment date. We included seven outcomes: 1) vaginal sex (yes/no); 2) number of vaginal sex partners (0–1 vs 2 or more); 3) "unsafe" vaginal sex (yes/no), defined as sex with a person of negative or unknown HIV serostatus, while viral load was not suppressed, without consistent condom use; 4) anal sex (yes/no); 5) number of anal sex partners (0–1 vs 2 or more); 6) "unsafe" anal (yes/no), defined as sex with a person of negative or unknown HIV serostatus, while viral load was not suppressed, without consistent condom use; and 7) sex under the influence of alcohol or drugs (yes/no).

Statistical Analysis

We analyzed person-periods for women, MSM, and MSW separately using non-drinking person-periods as the referent category. Risk ratios were estimated using log-linear models. We standardized person-periods within each alcohol use group to have the same distribution of potential confounders as the whole (stratum-specific) sample, so that differences in the relative risk (RR) of subsequent sexual behaviors were not due to confounding by measured covariates. We standardized using stabilized inverse probability of exposure weights (41,42). Inverse probability of exposure weights creates a pseudo-population in which the covariates used in the creation of the weights are not associated with exposure, and therefore cannot act as confounders. It does this by "upweighting" some persons with a pattern of covariates that is rare for his or her exposure group, and "downweighting" others with a pattern of covariates that are common for his or her exposure group.

Potential confounders included in the estimation of the weights were: age (and age squared); race/ethnicity; marijuana use; cocaine/crack use; illicit opioid use; methamphetamine use;

depressive symptoms; detectable viral load; and CNICS site. For some person-periods, not all risk behavior questions were answered and thus some outcomes were missing. We controlled for possibly differential probability of missing outcome data using stabilized inverse probability of censoring weights (43). Censoring weights were estimated conditional on reported alcohol use and the same set of covariates used in estimating inverse probability of exposure weights. Final weights were the product of inverse probability of exposure and inverse probability of censoring weights. Because some individuals contributed more than one person-period and their outcomes may be correlated, we fit models with generalized estimating equations (31) and an exchangeable covariance matrix.

To examine whether alcohol use interacted with cocaine/methamphetamine use or marijuana use to increase the probability of subsequent sexual behaviors, we estimated relative excess risk due to interaction (RERI) for each sexual behavior outcome (44,45). The prevalence of recent illicit opioid use was too low to estimate interactions between alcohol and opioid use. For these analyses, we collapsed person-periods into three categories of alcohol use at the start of the period: no use; moderate alcohol use (regardless of binge drinking); and hazardous alcohol use (regardless of binge drinking).

The RERI is a measure of departure from perfect additive interaction, expressed as a proportion of the risk in the doubly unexposed. For example, if we estimated that the RERI was 0 for anal sex comparing moderate drinking to non-drinking and cocaine use to non-use, then the risk of anal sex among women who drank moderately and used cocaine was equal to the risk incurred due to moderate drinking plus the risk incurred due to cocaine use. That is, at a population level, the risk associated with having more than one exposure was not more than the sum of the parts. A negative RERI indicates sub-additivity of risks while a positive RERI indicates super-additivity of risks (commonly referred to as synergism) (46). The doubly unexposed risk was defined as the risk of the outcome in person-periods with no baseline alcohol use and no baseline drug use. To avoid overinflating the relative excess risk of sex under the influence of drugs or alcohol due to interaction, the doubly “unexposed” risk was defined as the risk of the outcome in person-periods with moderate baseline alcohol use and no drug use. To control for confounding of the association between recreational drug use and subsequent sexual behaviors, we used a second set of inverse probability of exposure weights for the exposure of drug use. Weights were calculated similarly to the inverse probability of alcohol use exposure weights, but predictors excluded recreational drug use (since that was the dependent variable in the models). The final weights for the interaction models was the product of the two inverse probability of exposure weights and the inverse probability of censoring weights.

All statistical analyses were performed using STATA 14.1 (STATA Corp, College Station, TX, 2016). Statistical significance was set at α=0.05.

RESULTS

Participant Characteristics

The final study population included 1857 women, 6752 MSM and 2685 MSW (total=11,294 CNICS participants) who completed at least two PRO surveys between January 2011 and

June 2014. Table I shows baseline characteristics at first PRO, stratified by alcohol use pattern and sex/HIV acquisition risk factor for women, MSM, and MSW. The majority of women were black with median age in the early 40's. Median CD4 cells/μL ranged from 473 to 566 across categories of initial alcohol use, and slightly over a quarter of women (28.5%) had a detectable viral load at the time of the first person-period. The majority of MSM were white, median age in the early 40's, and median CD4 cells/μL ranging from 461 to 509 across categories of initial alcohol use at their first person-period. A quarter (25.2%) had a detectable viral load proximate to their initial PRO. The majority of MSW were black, with median age in the mid- to late 40's and median CD4 cells/μL ranging from 406 to 448 at their first PRO across categories of initial alcohol use. Slightly over a quarter (26.9%) had a detectable viral load proximate to their initial PRO.

The 12-month prevalence of alcohol use at first PRO for all study participants was: 36.2% no use; 30.0% moderate use without binge; 7.9% moderate use with binge; 5.6% hazardous use without binge; and 20.3% hazardous use with binge. Hazardous alcohol use (exceeding weekly limits) at the initial PRO was 18.6% among women, 29.4% among MSM and 22.0% among MSW. The prevalence of binge drinking (exceeding daily limits) was 14.11% among women, 33.3% among MSM and 25.2% among MSW.

At the first PRO, 3-month prevalence of cocaine/crack use was 7.5%, 6.0% and 10.5% among women, MSM and MSW, respectively. The 3-month prevalence of methamphetamine use was 2.7%, 11.2% and 10.5%, respectively. The 3-month prevalence of marijuana use was 14.4%, 33.2% and 26.0%, respectively. The 3-month prevalence of illicit opioid use was too low to estimate interactions between alcohol and opioid use, so it was not included in further analyses.

Table II shows the 6-month sexual behaviors at first PRO (outcomes) stratified by alcohol use pattern and sex/HIV acquisition risk factor for the 11,294 participants. Overall, the prevalence of any vaginal sex was 57.0% and 43.7% among women and MSW, respectively. The prevalence of vaginal sex with ≥2 partners was 6.3% and 7.6%, respectively. The prevalence of any anal sex was 7.7%, 54.8% and 20.7% among women, MSM and MSW, respectively. The prevalence of anal sex with ≥2 partners was 0.8%, 26.9% and 9.5%, respectively. The prevalence of unsafe vaginal sex was 2.6% among women and 1.4% among MSW, while the prevalence of unsafe anal sex was 0.3% among women, 3.3% among MSM and 1.0% among MSW. Finally, the prevalence of sex under the influence of drugs or alcohol among persons reporting any alcohol use at the index PRO was 29.2%, 42.1% and 40.5% among women, MSM and MSW, respectively.

Alcohol and recreational drug use across person-periods

We observed a total of 30,904 person-periods for the 11,294 participants (Table III). Median and interquartile range (interquartile range [IQR]) of number of person-periods per person was generally around 2 (1, 4) within each strata of women/MSM/MSW and alcohol use at the first PRO. The prevalence of hazardous alcohol use across all person-periods was 16.3% among women, 25.9% among MSM and 20.8% among MSW. The prevalence of binge drinking was 12.7% among women, 28.5% among MSM and 23.3% among MSW. These

proportions were similar to, but slightly below, the prevalence of hazardous and binge drinking at the first PRO for all groups.

Overall, prevalence of cocaine/crack use was 7.8%, 12.2% and 14.4% across person-periods contributed by women, MSM and MSW, respectively; among person-periods where hazardous drinking was reported at the index visit, prevalence of cocaine/crack use was 21.0%, 18.2% and 24.1% for women, MSM and MSW, respectively. Prevalence of recent marijuana use was 14.1%, 31.7% and 25.9% among women, MSM and MSW, respectively. Marijuana use was highest in person-periods where hazardous drinking was reported at the index visit: 32.7%, 44.6% and 41.8% for women, MSM and MSW, respectively.

Relationship between alcohol use and sexual behaviors across person-periods

Table IV summarizes multivariable models among women, MSM, and MSW. From multivariable models among women, any alcohol use was associated with an increased risk of subsequent vaginal sex, and there was some evidence to suggest that there was a relationship between a quantity/frequency increase of alcohol and subsequent vaginal sex: moderate drinking with and without binge drinking compared with no alcohol was associated with an RR = 1.17 (95% CI: 0.97, 1.42) and 1.13 (95% CI: 1.03, 1.24), respectively, while hazardous drinking with or without binge drinking was associated with an RR of 1.37 (95% CI: 1.21, 1.56) and 1.28 (95% CI: 1.12, 1.46), respectively. Any alcohol use (moderate drinking without binge: RR=1.46, 95% CI: 0.86, 2.45; moderate drinking with binge: RR= 1.18, 95% CI: 0.35, 3.94) and in particular hazardous alcohol use (without binge: RR= 2.41, 95% CI: 1.08, 5.38; with binge: RR = 2.16, 95% CI: 1.08, 4.35) was associated with greater risk of engaging in unsafe vaginal sex. Binge drinking did not appear to modify this excess risk of unsafe vaginal sex. There was strong evidence of an increase in quantity and frequency in alcohol use and its relationship risk of sex under the influence of drugs or alcohol. Specifically, risk was elevated for person-periods of moderate drinking relative to no drinking [with binge: RR =2.23, 95% CI: 1.08, 4.59; without binge RR=1.94, 95% CI: 1.32, 2.84], and the strongest association was with hazardous drinking (with binge: RR=5.47, 95% CI: 3.75, 7.99; without binge RR=5.18, 95% CI: 3.51, 7.63). For anal sex, anal sex with ≥ 2 partners, and particularly for unsafe anal sex, there were too few observations to determine whether there was an association between alcohol use and anal sex behaviors.

From multivariable models among MSM, there was evidence that alcohol use at the index visit was associated with an increased risk of subsequent anal sex and increased risk of anal sex with ≥2 partners relative to person-periods with no alcohol use. Moderate drinking (versus no drinking) was associated with having ≥2 anal sex partners (RR=1.33, 95% CI: 1.16, 1.52 and RR=1.18, 95% CI: 1.06, 1.31 with and without binge, respectively), and there was little evidence that hazardous drinking meaningfully increased the risk of ≥2 anal sex partners beyond moderate drinking with binge (RR=1.39, 95% CI: 1.34, 1.57 and RR=1.40, 95% CI: 1.21, 1.62, with and without binge, respectively). Moderate alcohol use was not statistically significantly associated with subsequent unsafe anal sex. Similar to women, there appeared to be a relationship between an increase in quantity/frequency of alcohol use and the subsequent risk of sex under the influence of drugs or alcohol. Any drinking versus

no drinking was associated with increased risk and the association seemed driven by number of drinks per week (i.e., greatest change in risk associated with moderate or hazardous drinking) rather than the presence or absence of binge drinking.

From multivariable models among MSW, alcohol use was associated with increased risk of subsequent anal sex and with increased risk of ≥2 anal sex partners; associations appeared to be driven primarily by binge drinking rather than number of drinks per week. MSW who reported any alcohol use had increased risk of subsequent vaginal sex. Reporting ≥2 vaginal sex partners was associated with hazardous drinking but not moderate drinking. Associations between alcohol use and engaging in unsafe anal sex were not significant. Risk of engaging in unsafe vaginal sex appeared to be most strongly driven by binge drinking (RR=3.12, 95% CI: 1.41, 6.94, for moderate drinking with binge, and RR=3.08, 95% CI: 1.57, 6.03 for hazardous drinking with binge) rather than by weekly quantity of drinks (RR=1.86, 95% CI: 0.98, 3.51 for moderate drinking without binge and RR=1.22, 95% CI: 0.29, 5.04 for hazardous drinking without binge. Finally, as seen in the other two subgroups, MSW who reported any alcohol use were more likely to report subsequent sex under the influence of drugs/alcohol, with higher risks associated with hazardous drinking.

Interaction between alcohol and drug use on sexual behaviors

We estimated additive interaction between alcohol use and cocaine/crack or methamphetamine use on risk of subsequent sexual behaviors. With the exception of risk of sex under the influence of drugs/alcohol among MSM, we observed no other significant departures from perfect additivity (Supplementary Table AI), indicating that alcohol and cocaine or methamphetamines act independently to increase risky sex. When we estimated additive interaction between alcohol use and marijuana use on risk of subsequent sexual behaviors, we estimated that the risk of subsequent vaginal sex among women was less than would be expected if hazardous drinking and marijuana use interacted additively. We saw no other statistically significant evidence of departure from perfect additivity for interactions between alcohol use and marijuana use (Supplementary Table AII).

DISCUSSION

In this cohort of 11,294 women, MSM and MSW who engaged in continuity HIV care across seven US clinical sites, we found that certain patterns of alcohol use were associated with an increased risk of subsequent sexual behaviors. Among women living with HIV, any alcohol use increased the likelihood of vaginal and unsafe vaginal sex. Hazardous alcohol use (for women >7 drinks/week) in particular increased the risk of vaginal sex, unsafe vaginal sex and when combined with binge drinking (for women: ≥4 drinks/occasion) increased the likelihood of having ≥2 vaginal sex partners. Among MSM, any alcohol use increased likelihood of having anal sex and ≥ 2 anal sex partners but was not associated with unsafe anal sex. Finally, among MSW, any alcohol use was associated with an increased risk of anal sex. However, binge drinking in particular (for men: ≥5 drinks/occasion) increased the risk of having ≥2 anal sex partners, ≥2 vaginal sex partners, vaginal sex, and unsafe vaginal sex. Across all PLWH groups, especially women, as the quantity and frequency of alcohol consumption increased, subsequent sex under the influence of alcohol or drugs

increased. Finally, we found that although alcohol and drug use were both prevalent and commonly co-occurring, there was little evidence that they interacted synergistically to increase sexual behaviors among PLWH. These findings have implications for counseling in HIV clinical care.

While our findings cannot isolate alcohol as a “cause” of sexual behaviors, our findings suggest that lifestyle patterns of drinking, previously shown to be quite stable in this cohort (47), increase the risk of certain sexual behaviors. Because these patterns differ between women, MSM and MSW, the groups may benefit from tailored counseling messages about alcohol use as part of sexual risk reduction. For women observing safer weekly limits of alcohol consumption and for MSW observing safer daily consumption limits seem warranted. For MSM, the counseling message would focus on increased risk of engaging in a variety of sexual behaviors from any alcohol use. Notably, however, alcohol use among MSM was not associated with an increased risk of unsafe anal sex. This suggests that compared with women and MSW, MSM may be more effectively reducing sexual transmission factors by reducing sex with partners of unknown or negative HIV serostatus, with a detectable viral load and/or inconsistent condom use.

For all PLWH groups, but especially for women, we found that the risk of having sex under the influence of drugs/alcohol markedly increases with increases in quantity and frequency of alcohol consumption. Laboratory and field studies have extensively documented alcohol and drug cognitive impairments on sexual expectations, decision-making, and consideration of consequences (12,14–16). Therefore, a “safe” level of alcohol use for some PLWH, perhaps especially for women, may be to abstain from alcohol especially in sexual contexts. For PLWH who are not ready or willing to abstain, drinking within safer limits of consumption may still reduce risk of harmful outcomes. Again, this may be particularly important for women who are more susceptible to the physiological effects of alcohol than men (48). Alcohol reduction to reduce sexual risk is important for women living with HIV because condom use is generally a more complex behavior for women and consequently behavioral interventions to promote their use have been less effective among women living with HIV than among men living with HIV (49). Finally, alcohol reduction is important for all PLWH who are taking multiple medications and have multiple comorbidities and who therefore may experience an exacerbation of alcohol’s effects through drug interactions and/or impaired hepatic metabolism (50–51). As behavioral interventions are still the mainstay of effective prevention, the challenge ahead will be to integrate the effective evidence-based interventions into routine clinical care.

Contrary to our earlier findings (11), anal sex among women living with HIV in this sample was reported infrequently and therefore there were too few outcomes to examine reliably. In our prior sample, 18% of Baltimore and New York women living with HIV reported anal sex, which was significantly associated with binge drinking. Although CNICS does include a Baltimore sample, 6 other US sites are also part of this cohort. We also predicted that binge drinking would be associated with elevated risk of sexual behaviors among women and MSM as has been reported in other studies (20,21). However, since we incorporated graphics to define types and amounts of alcohol contained in a “standard drink” into the PRO assessment, it is possible that we increased the precision of consumption estimates.

That is, an estimate of having “two drinks” on one occasion may be re-estimated as “four standard drinks” when the participant’s self-report is improved by the use of graphics. This may have lowered the threshold for detection of certain alcohol-associated sex behaviors.

Finally, although we found a high co-occurrence of alcohol and drug use among PLWH, we did not find that alcohol and drug use synergistically increased the probability of subsequent sexual transmission behaviors. This is particularly significant because it indicates that if the observed associations are causal then interventions to reduce alcohol use and drug use will both be necessary to reduce transmission sex in this population. The recommendation to address alcohol use separately from drug use to reduce sexual transmission behaviors is in line with recommendations to intervene separately on specific types of drug use to most effectively reduce drug-specific sexual transmission behaviors (32,52). For example, anal sex behaviors are associated with polydrug, marijuana, methamphetamine, illicit opioid and injection drug use whereas vaginal sex behaviors are associated with polydrug and crack cocaine use (20). Whether alcohol and drug use are optimally addressed simultaneously or sequentially will be determined in additional comparative efficacy research (19).

Limitations

We were unable to determine if the link between alcohol and sex is causal or mediated by a third factor, a confounder such as depression or sex-related alcohol expectancies. However, we were able to examine the link prospectively and found that alcohol use is a key temporal contributor to sexual behaviors. Second, our ability to directly estimate the effects of alcohol and drug use on HIV transmission was limited as we did not follow HIV uninfected partners of PLWH in our study. While we identified “unsafe sex” as inconsistent condom use with a partner of negative or unknown HIV serostatus while HIV viral load was not undetectable, it is possible that this unsafe sex may bave been misclassified as such if some of the HIV-uninfected partners were using pre-exposure prophylaxis. Pre-exposure prophylaxis would lower the likelihood of HIV acquisition, independent of the index HIV-infected partners’ plasma HIV RNA and sexual practices. Third, some of our subgroup analyses were limited in size and some of the sexual behaviors were infrequently reported, thus power to detect these associations was necessarily limited despite the large sample size. All classifications of person-periods with respect to alcohol consumption and drug use were based on self-report, and alcohol and drug use may have been underreported; however, we attempted to improve the accuracy of participants’ self-reported quantity of alcohol consumption by employing a graphic display of standard drinks prior to AUDIT-C completion. In past studies, where self-report queried only how many drinks were consumed, drinking amounts may have been underestimated (53). Fourth, an advantage of the PRO in CNICS is the geographic diversity of clinical sites, which can increase the generalizability of results. As we have previously shown, our findings about patients in CNICS generalize to other PLWH who are in care and not in CNICS (54). While we cannot generalize to PLWH not in care, a detectable viral load would be more likely and therefore alcohol misuse would potentially increase risk of HIV transmission. Finally, the PRO does not query detailed information about all sexual behaviors, the sex or gender of participants’ partners or consistently query across sites whether a participant is transgender female or male, although these as well as pre-exposure prophylaxis use by partners, and several other behaviors have been added more recently.

CONCLUSION

Among PLWH, identifiable patterns of alcohol use are associated with an increased risk of certain subsequent sex behaviors. These drinking patterns and sex behaviors differ however between women, MSM and MSW indicating the importance of tailored counseling messages about 'safer' alcohol use. For some PLWH, 'safer' alcohol consumption would include reductions in frequency and quantity of use and, for others, an alcohol-free lifestyle. Women living with HIV may benefit from tailored interventions that address their greater susceptibility to alcohol's effects, their risk of sex under the influence of drugs/alcohol with increased quantity and frequency of alcohol use, and the mixed results of prior interventions to promote condom use. For women, MSM, and MSW, alcohol and drug use did not synergistically increase the likelihood of subsequent sexual transmission behaviors; it also appears that separate interventions may be necessary to reduce sexual transmission behaviors. Optimizing the implementation of evidence-based interventions in HIV clinical settings is a critical next step in reducing alcohol use and sexual transmission behaviors among PLWH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I.

Characteristics of persons in continuity HIV care at a CNICS site, who completed at least two Patient Reported Outcomes (PRO) survey between January 2011 and June 2014, at first PRO, stratified by reported alcohol use and sex/HIV acquisition risk factor

	No alcohol use[a,b]	Moderate alcohol use/ no bingeing	Moderate alcohol use/ bingeing	Hazardous alcohol use/ no bingeing	Hazardous alcohol use/ bingeing
WOMEN (N=1857)	1010	449	52	136	210
Age, Median (IQR)[a]	43 (39, 53.5)	44 (35, 52)	39 (35, 49.5)	46 (38, 53)	44 (32, 51)
Race/ethnicity					
Black	658 (65.2)	280 (62.4)	32 (61.5)	89 (65.4)	108 (51.4)
White	236 (23.4)	125 (27.8)	14 (26.9)	18 (27.9)	60 (28.6)
Hispanic	88 (8.7)	31 (6.9)	4 (11.5)	5 (3.7)	27 (12.9)
Other	28 (2.8)	13 (2.9)	0 (0.0)	4 (2.9)	15 (7.1)
Depression (PHQ-2≥3)	170 (17.5)	91 (21.0)	18 (36.0)	36 (27.9)	67 (34.0)
Drug use in the last 3 months					
Cocaine/crack	39 (3.9)	31 (7.0)	5 (9.8)	20 (15.3)	45 (21.7)
Methamphetamines	18 (1.8)	14 (3.2)	4 (7.8)	3 (2.3)	11 (5.4)
Opioids	21 (2.1)	12 (2.8)	2 (3.8)	5 (4.0)	8 (3.9)
Marijuana	63 (6.4)	92 (21.3)	10 (19.6)	31 (23.8)	72 (35.8)
Injection drugs	8 (1.2)	4 (1.1)	0 (0.0)	2 (1.8)	4 (2.7)
CD4 cells/μL, Median (IQR)[a]	510.5 (301, 732)	535 (325.5, 708)	558 (315, 834)	566 (347, 789)	473 (268, 676)
Viral load >100 copies/mL (detectable)	263 (26.1)	131 (29.2)	12 (23.1)	38 (28.2)	86 (41.0)
MSM (N=6752)	1871	2246	648	384	1603
Age, Median (IQR)[a]	45 (38, 51)	44 (34, 51)	39 (32, 46)	44 (32, 50)	41 (31, 47)
Race/ethnicity					
Black	470 (25.1)	523 (23.3)	119 (18.4)	85 (22.1)	272 (17.0)
White	974 (52.1)	1299 (57.8)	375 (57.9)	228 (59.4)	953 (59.5)
Hispanic	322 (17.2)	313 (13.9)	104 (16.1)	48 (12.5)	302 (18.8)
Other	105 (5.6)	111 (4.9)	50 (7.7)	23 (6.0)	76 (4.7)
Depression (PHQ-2≥3)	437 (23.7)	462 (20.9)	128 (20.1)	78 (20.6)	364 (23.1)
Drug use in the last 3 months					

	No alcohol use[a,b]	Moderate alcohol use/ no bingeing	Moderate alcohol use/ bingeing	Hazardous alcohol use/ no bingeing	Hazardous alcohol use/ bingeing
Cocaine/crack	50 (2.7)	95 (4.3)	33 (5.1)	34 (9.5)	195 (12.3)
Methamphetamines	190 (10.3)	234 (10.6)	98 (15.5)	34 (9.5)	198 (12.4)
Opioids	22 (1.2)	24 (1.1)	13 (2.0)	4 (1.1)	35 (2.2)
Marijuana	354 (19.2)	744 (34.0)	266 (41.8)	142 (39.7)	735 (46.9)
Injection drugs	6.0 (3.5)	57 (2.7)	18 (2.9)	8 (2.3)	43 (2.8)
CD4 cells/μL, Median (IQR)[a]	461.5 (286, 651)	492 (318, 676)	509 (347, 688)	499 (327, 692)	484 (323, 666)
Viral load >100 copies/mL (detectable)	447 (23.9)	547 (24.4)	170 (26.3)	83 (21.7)	453 (28.3)
MSW (N=2685)	1209	690	194	110	482
Age, Median (IQR)[a]	49 (41, 56)	47 (39, 52.5)	41 (34, 50)	44 (36, 50)	44 (35, 50)
Race/ethnicity					
Black	638 (52.8)	323 (46.8)	64 (33.0)	56 (50.9)	189 (39.2)
White	391 (32.3)	271 (39.3)	92 (47.4)	44 (40.0)	208 (43.2)
Hispanic	145 (12.0)	70 (10.1)	32 (16.5)	8 (7.3)	58 (12.0)
Other	35 (2.9)	26 (3.8)	6 (3.1)	2 (1.8)	27 (5.6)
Depression (PHQ-2≥3)	223 (19.0)	145 (21.8)	43 (23.6)	18 (17.0)	120 (26.4)
Drug use in the last 3 months					
Cocaine/crack	66 (5.5)	63 (9.4)	27 (14.1)	13 (13.1)	112 (23.6)
Methamphetamines	80 (6.8)	89 (13.2)	36 (18.8)	7 (7.1)	70 (14.9)
Opioids	39 (3.3)	46 (6.9)	17 (9.0)	4 (4.2)	48 (10.2)
Marijuana	174 (14.9)	209 (31.6)	73 (39.2)	40 (40.8)	201 (49.1)
Injection drugs	48 (5.8)	48 (8.6)	21 (12.9)	5 (5.6)	31 (7.8)
CD4 cells/μL, Median (IQR)[a]	415 (245, 626)	425 (250, 655)	406 (244, 620)	448.5 (238, 657)	421 (247, 588)
Viral load >100 copies/mL (detectable)	284 (23.6)	175 (25.4)	70 (36.1)	33 (30.0)	161 (33.5)

Abbreviations: IQR, interquartile range; MSM, men who have sex with men; MSW, men who have sex with women

[a] N(%) unless otherwise indicated

[b] Moderate alcohol use defined as more than 0 but <7/<14 drinks per week for men/women, on average; Hazardous alcohol use defined as >7/>14 drinks per week for women/men, on average; Binge drinking defined as drinking ≥ 4/≥5 drinks on one occasion for women/men.

Table II.

Sexual behaviors of persons in continuity HIV care at a CNICS site at first PRO stratified by alcohol use pattern and reported sex/HIV acquisition risk factor

	No alcohol use[a,b]	Moderate alcohol use/ no bingeing	Moderate alcohol use/ bingeing	Hazardous alcohol use/ no bingeing	Hazardous alcohol use/ bingeing
WOMEN (N=1857)	1010	449	52	136	210
Vaginal sex	472 (56.4)	284 (67.3)	30 (66.7)	80 (63.0)	138 (74.6)
≥2 vaginal sex partners	41 (4.9)	43 (10.2)	2 (4.4)	9 (7.1)	23 (12.4)
Unsafe vaginal sex	24 (2.7)	17 (4.3)	0 (0.0)	7 (6.0)	9 (5.3)
Anal sex	56 (6.9)	35 (8.6)	4 (9.1)	16 (13.0)	30 (16.9)
≥2 anal sex partners	9 (1.1)	4 (1.0)	1 (2.3)	2 (1.6)	5 (2.8)
Unsafe anal sex	2 (0.2)	0 (0.0)	0 (0.0)	2 (1.5)	6 (3.0)
Sex under influence of alcohol/drugs	33 (6.0)	64 (19.9)	5 (15.2)	42 (45.2)	69 (48.6)
MSM (N=6752)	1871	2246	648	384	1603
Anal sex	783 (45.3)	1278 (60.3)	441 (71.6)	223 (60.9)	1044 (69.1)
≥2 anal sex partners	427 (24.7)	628 (29.7)	236 (38.3)	133 (36.3)	622 (41.2)
Unsafe anal sex	73 (4.2)	110 (5.4)	31 (5.3)	29 (8.1)	110 (7.8)
Sex under influence of alcohol/drugs	217 (14.4)	584 (30.3)	271 (46.9)	164 (53.4)	877 (62.3)
MSW (N=2685)	1209	690	194	110	482
Vaginal sex	462 (45.5)	272 (43.2)	68 (38.0)	48 (47.1)	206 (46.1)
≥2 vaginal sex partners	73 (7.2)	46 (7.8)	14 (7.8)	10 (9.8)	59 (13.2)
Unsafe vaginal sex	13 (1.2)	11 (1.8)	5 (2.8)	4 (4.1)	12 (2.8)
Anal sex	148 (14.8)	157 (25.2)	66 (37.5)	24 (23.5)	134 (30.2)
≥2 anal sex partners	76 (7.6)	70 (11.2)	42 (23.9)	12 (11.8)	67 (15.1)
Unsafe anal sex	12 (1.1)	8 (1.2)	6 (3.5)	3 (2.9)	12 (2.8)
Sex under influence of alcohol/drugs	95 (13.6)	147 (30.2)	66 (44.6)	50 (60.2)	202 (57.2)

Abbreviations: MSM, men who have sex with men; MSW, men who have sex with women

[a] N (%) unless otherwise indicated

[b] Moderate alcohol use defined as more than 0 but ≤7/≤14 drinks per week for men/women, on average; Hazardous alcohol use defined as >7/>14 drinks per week for women/men, on average; Binge drinking defined as drinking ≥ 4/≥5 drinks on one occasion for women/men.

Table III.

Characteristics of person-periods that occur over within Patient Reported Outcomes (PRO) survey between January 2011 and June 2014, at first PRO, stratified by reported alcohol use and sex/HIV acquisition risk factor

	No alcohol use[a,b]	Moderate alcohol use/ no bingeing	Moderate alcohol use/ bingeing	Hazardous alcohol use/ no bingeing	Hazardous alcohol use/ bingeing
WOMEN					
Number of person-periods (N=5281)	2931	1342	147	336	525
Person-periods/person, Median (IQR)[a]	2 (1, 4)	2 (1, 4)	2 (1, 5)	1 (1, 3)	2 (1, 4)
MSM					
Number of person-periods (N=18533)	5507	6568	1657	1185	3616
Observations/person, Median (IQR)[a]	2 (1, 4)	2 (1, 4)	2 (1, 4)	2 (1, 2)	2 (1, 4)
MSW					
Number of person-periods (N=7090)	3255	1874	486	311	1164
Observations/person, Median (IQR)[a]	2 (1, 4)	2 (1, 4)	2 (1, 4)	1 (1, 2)	2 (1, 4)

Abbreviations: IQR, interquartile range; MSM, men who have sex with men; MSW, men who have sex with women

[a]Moderate alcohol use defined as more than 0 but ≤7/≤14 drinks per week for men/women, on average; Hazardous alcohol use defined as >7/>14 drinks per week for women/men, on average; Binge drinking defined as drinking ≥ 4/≥5 drinks on one occasion for women/men.

Table IV.

Risk ratios and 95% confidence limits for seven subsequent sexual behaviors associated with different levels of self-reported alcohol use[a] among 11,294 women, men who have sex with men (MSM) and men who have sex with women (MSW) in CNICS observed for 30,904 person-periods

	Women	MSM	MSW
Anal sex			
No alcohol use	1.	1.	1.
Moderate drinking without binge	0.99 (0.69 , 1.41)	**1.26 (1.19 , 1.34)**	**1.30 (1.09 , 1.55)**
Moderate drinking with binge	0.88 (0.45 , 1.73)	**1.33 (1.24 , 1.44)**	**1.62 (1.28 , 2.06)**
Hazardous drinking without binge	0.99 (0.57 , 1.70)	**1.28 (1.18 , 1.39)**	1.23 (0.84 , 1.79)
Hazardous drinking with binge	2.22 (0.92 , 5.36)	**1.32 (1.23 , 1.42)**	**1.42 (1.15 , 1.77)**
≥2 anal sex partners			
No alcohol use	1.	1.	1.
Moderate drinking without binge	0.62 (0.16 , 2.39)	**1.18 (1.06 , 1.31)**	1.18 (0.91 , 1.52)
Moderate drinking with binge	0.36 (0.04 , 3.03)	**1.33 (1.16 , 1.52)**	**1.82 (1.29 , 2.58)**
Hazardous drinking without binge	1.28 (0.34 , 4.79)	**1.40 (1.21 , 1.62)**	1.15 (0.56 , 2.34)
Hazardous drinking with binge	1.50 (0.50 , 4.56)	**1.39 (1.24 , 1.57)**	**1.52 (1.11 , 2.07)**
Vaginal sex			
No alcohol use	1.		1.
Moderate drinking without binge	**1.13 (1.03 , 1.24)**		1.10 (0.99 , 1.22)
Moderate drinking with binge	1.17 (0.97 , 1.42)		1.14 (0.98 , 1.33)
Hazardous drinking without binge	**1.28 (1.12 , 1.46)**		1.01 (0.80 , 1.27)
Hazardous drinking with binge	**1.37 (1.21 , 1.56)**		**1.19 (1.05 , 1.35)**
≥2 vaginal sex partners			
No alcohol use	1.		1.
Moderate drinking without binge	**1.53 (1.08 , 2.18)**		0.98 (0.74 , 1.31)
Moderate drinking with binge	0.90 (0.37 , 2.20)		1.07 (0.67 , 1.73)
Hazardous drinking without binge	0.99 (0.50 , 1.97)		0.88 (0.50 , 1.54)
Hazardous drinking with binge	**2.06 (1.21 , 3.50)**		**1.69 (1.25 , 2.29)**
Sex under influence of drugs/alcohol			
No alcohol use	1.	1.	1.
Moderate drinking without binge	**1.94 (1.32 , 2.84)**	**1.76 (1.53 , 2.02)**	**1.78 (1.47 , 2.16)**
Moderate drinking with binge	**2.23 (1.08 , 4.59)**	**2.36 (2.03 , 2.74)**	**2.26 (1.78 , 2.87)**
Hazardous drinking without binge	**5.18 (3.51 , 7.63)**	**3.01 (2.58 , 3.51)**	**2.67 (1.99 , 3.58)**
Hazardous drinking with binge	**5.47 (3.75 , 7.99)**	**3.22 (2.81 , 3.70)**	**3.15 (2.59 , 3.83)**
Unsafe[b] anal sex			
No alcohol use	1.	1.	1.
Moderate drinking without binge	0.26 (0.02 , 3.74)	1.07 (0.72 , 1.60)	1.02 (0.45 , 2.29)
Moderate drinking with binge	0.88 (0.06 , 12.86)	1.05 (0.62 , 1.78)	1.56 (0.59 , 4.16)
Hazardous drinking without binge	0.95 (0.09 , 10.24)	1.24 (0.73 , 2.09)	1.60 (0.50 , 5.13)
Hazardous drinking with binge	2.63 (0.34 , 20.43)	1.30 (0.86 , 1.98)	1.46 (0.61 , 3.47)

	Women	MSM	MSW
Unsafe[b] vaginal sex			
No alcohol use	1.		1.
Moderate drinking without binge	1.46 (0.86 , 2.45)		1.86 (0.98 , 3.51)
Moderate drinking with binge	1.18 (0.35 , 3.94)		**3.12 (1.41 , 6.94)**
Hazardous drinking without binge	**2.41 (1.08 , 5.38)**		1.22 (0.29 , 5.04)
Hazardous drinking with binge	**2.16 (1.08 , 4.35)**		**3.08 (1.57 , 6.03)**

[a]Moderate alcohol use defined as more than 0 but ≤7/≤14 drinks per week for men/women, on average; Hazardous alcohol use defined as >7/>14 drinks per week for women/men, on average; Binge drinking defined as drinking ≥ 4/≥5 drinks on one occasion for women/men.

[b]"Unsafe" sex was defined as sex with a person of unknown or negative HIV serostatus, with a recent detectable viral load, and with inconsistent condom use

Bolded findings are significant at α=0.05.