CFAR Substance Use Research Core (SURC) Faculty Publication and New Awards Digest

New research on HIV and substance use by our SURC faculty.

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New Grants Awarded

Mobile health intervention to increase HIV self testing and linkage to services for high-risk men in China.

R01MH123352 (D Operario)   **4/1/2020-1/31/2025**

The overarching goal of this research is to advance the science of mobile health approaches to increase uptake of repeat HIV self-testing (HST) and linkage to HIV-related care with populations that underperform on these steps of the HIV care continuum. These findings will be crucial for optimizing the care cascade in populations that underutilize HIV services, such as MSM in China and elsewhere in the world where HIV testing and linkage to care services are sub-optimal.

New Publications

Alcohol and bone turnover markers among people living with HIV and substance use disorder.

Kim TW, Ventura AS, Winter MR, Heeren TC, Holick MF, **Walley AY**, Bryant KJ, **Saitz R**. Alcohol Clin Exp Res. 2020;10.1111/acer.14303.

Background:
Although unhealthy alcohol use and low bone density are prevalent among people living with HIV (PLWH), it is not clear whether alcohol use is associated with bone turnover markers (BTMs), and if so, at what quantity and frequency. The study objective was to examine the association between alcohol and BTMs in PLWH with substance use disorder.

Methods:
We studied a prospective cohort recruited from 2 HIV clinics who met criteria for DSM-IV substance

dependence or reported ever injection drug use. Outcomes were BTM of (i) bone formation (serum procollagen type 1 N-terminal propeptide [P1NP]) and (ii) bone resorption (serum C-telopeptide type 1 collagen [CTx]). Alcohol consumption measures included (i) mean number of drinks/d (Timeline Follow-Back [TLFB]) (primary predictor), (ii) any alcohol use on ≥20 of the past 30 days, and phosphatidylethanol (PEth), a biomarker of recent alcohol consumption. Linear regression analysis examined associations between (i) each alcohol measure and each BTM and (ii) change in alcohol and change in BTM over 12 months.

Results:
Among 198 participants, baseline characteristics were as follows: The median age was 50 years; 38% were female; 93% were prescribed antiretroviral medications; 13% had ≥20 drinking days/month; mean drinks/day was 1.93 (SD 3.89); change in mean drinks/day was -0.42 (SD 4.18); mean P1NP was 73.1 ng/ml (SD 34.5); and mean CTx was 0.36 ng/ml (SD 0.34). Higher drinks/day was significantly associated with lower P1NP (slope -1.09 ng/ml; 95% confidence interval [CI] -1.94, -0.23, per each additional drink). On average, those who drank on ≥ 20 days/month had lower P1NP (-15.45 ng/ml; 95% CI: -26.23, -4.67) than those who did not. Similarly, PEth level ≥ 8ng/ml was associated with lower P1NP. An increase in drinks/d was associated with a decrease in P1NP nonsignificantly (-1.14; 95% CI: -2.40, +0.12; p = 0.08, per each additional drink). No significant associations were detected between either alcohol measure and CTx.

Conclusions:
In this sample of PLWH with substance use disorder, greater alcohol consumption was associated with lower serum levels of bone formation markers.

Examination of using alcohol to cope, depressive symptoms, and perceived social support in persons with HIV and Hepatitis C.

Moitra E, Anderson BJ, Herman DS, Hayaki J, Pinkston MM, Kim HN,**Stein MD**. AIDS Care. 2020;1–8.

Depression is common among people living with HIV (PLWH) and some likely turn to alcohol to cope with this emotional distress. Using alcohol to cope is associated with increased alcohol use, persistent longitudinal alcohol use, and alcohol-related problems. This association is particularly concerning among PLWH who are co-infected with Hepatitis C (HCV) because alcohol adds to the damage already caused by HCV. Despite data showing the associated risks of using alcohol to cope, scant research has examined factors that might contribute to coping-based alcohol use in HIV-HCV patients, such as limited social support. Baseline data from a randomized trial of strategies to reduce alcohol use in co-infected HIV and HCV adult patients (n=110) were analyzed. Multiple linear regression models were used to estimate the association between using alcohol to cope, depression, and four aspects of social support, controlling for demographic variables. Results showed that using alcohol to cope was not significantly correlated with social support but was significantly correlated with depressive symptoms. In fact, depressive symptoms and severity of alcohol consumption accounted for nearly 45% of the variance related to coping-based alcohol use. These data highlight the central role of depression in the coping motives-alcohol use relationship among co-infected patients.

HIV and cardiovascular disease.

So-Armah K, Benjamin L, Bloomfield G, Feinstein M, Hsue P, Njuguna B, Freiberg M.The Lancet. 2020; 7(4):e279-e293.

HIV-related cardiovascular disease research is predominantly from Europe and North America. Of the estimated 37·9 million people living with HIV worldwide, 25·6 million live in sub-Saharan Africa. Although mechanisms for HIV-related cardiovascular disease might be the same in all people with HIV, the distribution of cardiovascular disease risk factors varies by geographical location. Sub-Saharan Africa has a younger population, higher prevalence of elevated blood pressure, lower smoking rates, and lower prevalence of elevated cholesterol than western Europe and North America. These variations mean that the profile of cardiovascular disease differs between low-income and high-income countries. Research in, implementation of, and advocacy for risk reduction of cardiovascular disease in the global context of HIV should account for differences in the distribution of traditional cardiovascular disease risk factors (eg, hypertension, smoking), consider non-traditional cardiovascular disease risk factors (eg, access to antiretroviral therapy with more benign cardiovascular disease side effect profiles, indoor air pollution), and encourage the inclusion of relevant risk reduction approaches for cardiovascular disease in HIV-care guidelines. Future research priorities include implementation science to scale up and expand integrated HIV and cardiovascular disease care models, which have shown promise in sub-Saharan Africa; HIV and cardiovascular disease epidemiology and mechanisms in women; and tobacco cessation for people living with HIV.

Poor sleep health is associated with increased mental health problems,

substance use, and HIV sexual risk behavior in a large, multistate sample of gay, bisexual and other men who have sex with men (GBMSM) in Nigeria, Africa.

Ogunbajo A**,** Restar A, Edeza A, Goedel W, Jin H, Iwuagwu S, Williams R, Abubakari MR, Biello K, **Mimiaga M**. Sleep Health. 2020;S2352-7218(20)30076-0.

Background:
Poor sleep health has been linked to mental health problems, substance use, and sexual risk-taking among gay, bisexual, and other men who have sex with men (GBMSM). No known published study has examined these relationships among African GBMSM. Consequently, we investigated poor sleep health and associated health-related factors among a large multistate sample of Nigerian GBMSM.

Methods:
Between March and June 2019, 406 GBMSM were recruited from Abuja, Delta, Lagos, and Plateau and asked to complete an interviewer-administered survey. Bivariate and multivariable logistic regression models were constructed to examine the relationship between poor sleep health and other health-related factors.

Results:
In the past month, 45.5% of participants reported sleeping an average of 6 hours or less every night, and 30.7% reported experiencing a sleep problem. Factors associated with increased odds of reporting short sleep included: residing in Delta [adjusted odds ratio (aOR) 2.16; 95% confidence interval (CI): 1.15 to 4.04] and Lagos (aOR 2.40; 95% CI: 1.29 to 4.45), depressive symptoms (aOR 1.94; 95% CI: 1.13 to 3.32), and reporting lifetime history of using four or more drugs (aOR 2.52; 95% CI: 1.06 to 6.01). Reporting condom use at last anal sex was associated with decreased odds of reporting short sleep in the last month (aOR 0.54; 95% CI: 0.31 to 0.92). Factors associated with increased odds of reporting sleep problems included: reporting an STI diagnosis in the last year (aOR 1.79; 95% CI: 1.05 to 3.05) and reporting monthly or higher polydrug use in the last 3 months (aOR 2.19; 95% CI: 1.14 to 4.24).

Discussion:
Sleep health interventions should be developed for Nigerian GBMSM, which may improve mental health and reduce substance use and sexual risk-taking.

Predictors of initiation of and retention on medications for alcohol use disorder among people living with and without HIV.

Oldfield BJ, McGinnis KA, Edelman EJ, Williams EC, Gordon AJ, Akgün K, Crystal S, Fiellin LE, Gaither JR, Goulet JL, Korthuis PT, **Marshall BDL**, Justice AC, Bryant K, Fiellin DA, Kraemer KL.J Subst Abuse Treat. 2020;109:14–22.

Introduction:
Infrequent use of and poor retention on evidence-based medications for alcohol use disorder (MAUD) represent a treatment gap, particularly among people living with HIV (PLWH). We examined predictors of MAUD initiation and retention across HIV status.

Methods:
From Veterans Aging Cohort Study (VACS) data, we identified new alcohol use disorder (AUD) diagnoses from 1998 to 2015 among 163,339 individuals (50,826 PLWH and 112,573 uninfected, matched by age, sex, and facility). MAUD initiation was defined as a prescription fill for naltrexone, acamprosate or disulfiram within 30 days of a new diagnosis. Among those who initiated, retention was defined as filling medication for ≥80% of days over the following six months. We used multivariable logistic regression to assess patient- and facility-level predictors of AUD medication initiation across HIV status.

Results:
Among 10,603 PLWH and 24,424 uninfected individuals with at least one AUD episode, 359 (1.0%) initiated MAUD and 49 (0.14%) were retained. The prevalence of initiation was lower among PLWH than those without HIV (adjusted odds ratio [AOR] 0.66, 95% confidence interval [CI] 0.51-0.85). Older age (for PLWH: AOR 0.78, 95% CI 0.61-0.99; for uninfected: AOR 0.70, 95% CI 0.61-0.80) and black race (for PLWH: AOR 0.63, 95% CI 0.0.49-0.1.00; for uninfected: AOR 0.63, 95% CI 0.48-0.83), were associated with decreased odds of initiation for both groups. The low frequency of retention precluded multivariable analyses for retention.

Conclusions:
For PLWH and uninfected individuals, targeted implementation strategies to expand MAUD are needed, particularly for specific subpopulations (e.g. black PLWH).

Recreational use of HIV antiretroviral medication and implications for HIV

pre-exposure prophylaxis and treatment.
Kuo C, Giovenco D, DeAtley T, Hoare J, Underhill K, Atujuna M, Mathews C, Stein DJ, Brown LK, **Operario D**. AIDS Behav. 2020;10.1007/s10461-020-02821-5.

Diversion of antiretroviral therapy (ART) for recreational use is concerning for countries with high HIV prevalence. This paper presents reports of recreational use of ART among adolescents from two HIV prevention studies in South Africa: (1) a cross-sectional survey of N = 200 adolescents and (2) a qualitative study of pre-exposure prophylaxis with N = 57 adolescents and N = 25 clinicians. Among adolescents, 3% used and 14% knew someone who used non-prescribed ART for recreational purposes. Administration included smoking (71%), snorting (15%), injecting (15%), ingesting (15%), and inserting (3%). Participants predicted increased crime as recreational use of ART increased. Future studies should investigate prevalence, composition, and diversion of ART from HIV prevention and treatment.

Tutorial in Biostatistics: The use of generalized additive models to evaluate alcohol consumption as an exposure variable.
White LF, Jiang W, Ma Y, **So-Armah K**, **Samet JH**, Cheng DM. Drug Alcohol Depend. 2020;209:107944.

Alcohol consumption is a commonly studied risk factor for many poor health outcomes. Various instruments exist to measure alcohol consumption, including the AUDIT-C, Single Alcohol Screening Questionnaire (SASQ) and Timeline Followback. The information gathered by these instruments is often simplified and analyzed as a dichotomous measure, risking the loss of information of potentially prognostic value. We discuss generalized additive models (GAM) as a useful tool to understand the association between alcohol consumption and a health outcome. We demonstrate how this analytic strategy can guide the development of a regression model that retains maximal information about alcohol consumption. We illustrate these approaches using data from the Russia ARCH (Alcohol Research Collaboration on HIV/AIDS) study to analyze the association between alcohol consumption and biomarker of systemic inflammation, interleukin-6 (IL-6). We provide SAS and R code to implement these methods. GAMs have the potential to increase statistical power and allow for better elucidation of more nuanced and non-linear associations between alcohol consumption and important health outcomes.

Using ecological momentary assessment (EMA) to explore mechanisms of alcohol-involved HIV risk behavior among men who have sex with men (MSM).
Wray TB, **Monti PM**, **Kahler CW**, Guigayoma JP. Addiction. 2020;10.1111/add.15053.

Background and Aims:
Heavy drinking is associated with increased risk of incident HIV infection among men who have sex with men (MSM). Past studies suggest that this association may be due to the tendency for intoxication to interfere with condom use. However, research on potential causal mechanisms explaining this relationship has been limited primarily to laboratory studies. In this study, we tested several potential mediators of the relationship between alcohol use level and HIV risk behavior.

Design:
Ecological momentary assessment (EMA) methods conducted over a 30-day period.
Setting and participants/cases: MSM (n = 100) in the northeastern United States.
Measurements: Participants completed daily diary surveys and up to six experience sampling surveys randomly prompted throughout the day.

Findings:
Very heavy levels of drinking (12+ drinks) increased the odds of engaging in any sex [odds ratio (OR) = 1.87, P < 0.001]. Coefficient products and 95% confidence intervals indicated that both subjective sexual arousal (OR = 1.52, P < 0.001) and sex intentions (OR = 1.74, P < 0.001) significantly mediated the association between very heavy drinking and the odds of sex. When participants reported sex, the odds of engaging in high-risk condomless anal sex (CAS) increased incrementally after drinking heavily (five to 11 drinks; OR = 3.27, P = 0.006) and very heavily (12+ drinks; OR = 4.42, P < 0.001). Only subjective sexual arousal significantly mediated the association between alcohol use level and high-risk CAS (OR = 1.16, P = 0.040).

Conclusions:
Increases in subjective sexual arousal after drinking heavily appear to partly account for alcohol-related HIV risk behaviors in the daily lives of men who have sex with men. Alcohol's role in strengthening motivationally consistent emotional states may therefore play a more important role in facilitating alcohol-involved HIV risk than explicit sexual motivation.