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

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

If you have any other publications or awards, please send them toNatalia Gnatienko to include in the next publication digest!

Please remember to cite CFAR support (P30AI042853) on your future publications!

Visit the SURC webpage

Announcements

Jeffrey Samet Receives CPDD Award for Excellence

SURC faculty member Dr. Jeffrey Samet, MD, MA, MPH, is a 2024 recipient of the College on Problems of Drug Dependence (CPDD) Award for Excellence. Dr. Samet is the John Noble, M.D. Professor in General Internal Medicine and Professor of Public Health at Boston University Chobanian and Avedisian School of Medicine and School of Public Health. Dr. Samet will receive the James L. Sorensen Distinguished Treatment & Service Mentor Award at the 2024 CPDD Annual Meeting. Congratulations, Jeffrey!

Early Stage Investigator Opportunities

The Inter-CFAR Substance Use Research Community (I-SURC) Early Stage Investigator Spotlight Seminar Series aims to provide a platform for early stage investigators to disseminate their work to a national audience of investigators with specific interests in the intersection of HIV and substance use. This opportunity is reserved for early career investigators (post-doctoral fellow or faculty at the Assistant Professor level), who

would like to present work that has either not yet been published or was published less than a year ago. If you are interested in being considered for this opportunity, please complete this brief form.

Additionally, the I-SURC Steering Committee provides feedback on grant applications in development and can match investigators with mentors in a requested area of HIV and substance use research. Grant feedback opportunities are available for early stage investigators who have not received R01 funding and are submitting a K-series or first R-series award. If you are interested, please click here.

Recent Funding Announcements

RFA-DA-25-060: High Priority HIV and Substance Use Research (RM1 Clinical Trial Optional)

RFA-DA-22-040: High Priority HIV and Substance Use Research (R01 Clinical Trial Optional)

RFA-MH-25-185: Advancing HIV service delivery through pharmacies and pharmacists (R01 Clinical Trial Optional)

RFA-MH-25-186: Advancing HIV service delivery through pharmacies and pharmacists (R21 Clinical Trial Optional)

RFA-DA-25-004: Research on the Neuro-Immune Axis in the context of HIV and Substance Use (R01 Clinical Trial Not Allowed)

RFA-DA-25-005: Research on the Neuro-Immune Axis in the Context of HIV and Substance Use (R21 Clinical Trial Not Allowed)

View more NIDA funding opportunities at the intersection of HIV and substance use here.

Please let us know if you are interested in pursuing these opportunities!

New Publications

Experimentally induced reductions in alcohol consumption and brain, cognitive, and clinical outcomes in older persons with and those without HIV infection (30-Day Challenge Study): protocol for a nonrandomized clinical trial. *JMIR Res Protoc*. 2024 Apr 2;13:e53684. PMCID: PMC11028398.
Cook RL, Richards VL, Gullett JM, Lerner BDG, Zhou Z, Porges EC, Wang Y, **Kahler CW**, Barnett NP, Li Z, Pallikkuth S, Thomas E, Rodriguez A, Bryant KJ, Ghare S, Barve S, Govind V, Dévieux JG, Cohen RA; 30-Day Challenge Research Team.

Background: Both alcohol consumption and HIV infection are associated with worse brain, cognitive, and clinical outcomes in older adults. However, the extent to which brain and cognitive dysfunction is reversible with reduction or cessation of drinking is unknown.
Objective: The 30-Day Challenge study was designed to determine whether reduction or cessation of drinking would be associated with improvements in cognition, reduction of systemic and brain inflammation, and improvement in HIV-related outcomes in adults with heavy drinking.
Methods: The study design was a mechanistic experimental trial, in which all participants

received an alcohol reduction intervention followed by repeated assessments of behavioral and clinical outcomes. Persons were eligible if they were 45 years of age or older, had weekly alcohol consumption of 21 or more drinks (men) or 14 or more drinks (women), and were not at high risk of alcohol withdrawal. After a baseline assessment, participants received an intervention consisting of contingency management (money for nondrinking days) for at least 30 days followed by a brief motivational interview. After this, participants could either resume drinking or not. Study questionnaires, neurocognitive assessments, neuroimaging, and blood, urine, and stool samples were collected at baseline, 30 days, 90 days, and 1 year after enrollment.
Results: We enrolled 57 persons with heavy drinking who initiated the contingency management protocol (mean age 56 years, SD 4.6 years; 63%, n=36 male, 77%, n=44 Black, and 58%, n=33 people with HIV) of whom 50 completed 30-day follow-up and 43 the 90-day follow-up. The planned study procedures were interrupted and modified due to the COVID-19 pandemic of 2020-2021.
Conclusions: This was the first study seeking to assess changes in brain (neuroimaging) and cognition after alcohol intervention in nontreatment-seeking people with HIV together with people without HIV as controls. Study design strengths, limitations, and lessons for future study design considerations are discussed. Planned analyses are in progress, after which deidentified study data will be available for sharing.

Socioeconomic status and CD4 count among people with HIV who inject drugs in St. Petersburg, Russia. *AIDS Behav*. 2024 Apr 24. Epub ahead of print.
Idrisov B, Van Draanen J, Lodi S, **Lunze K**, Kimmel SD, Quinn EK, Truong V, Blokhina E, Gnatienko N, Krupitsky E, **Samet JH**, Williams EC.

Lack of access to resources is a "fundamental cause" of poor HIV outcomes across the care cascade globally and may have the greatest impact on groups with co-existing marginalized identities. In a sample of people living with HIV (PWH) who inject drugs and were not on antiretroviral therapy (ART), we explored associations between access to resources and HIV severity. Fundamental Cause Theory (FCT) sees socioeconomic status/access to resources as a root cause of disease and emphasizes that individuals with limited resources have fewer means to mitigate health risks and implement protective behaviors, which ultimately generates disparities in health outcomes. Guided by the FCT, we hypothesized that resource depletion (primary aim) and lower income (secondary aim) were associated with increased HIV severity. Using baseline data from the Linking Infectious and Narcology Care (LINC-II) trial of ART-naive PWH who inject drugs in St. Petersburg, Russia (n = 225), we examined the association between "past year resource runout" (yes vs. no) and "low-income (< 300 USD a month)" and the outcome HIV severity (CD4 count, continuous). We fit two separate linear regression models adjusted for gender, age, time since HIV diagnosis, and prior ART use. Participants had a mean age of 37.5 years and were 60% male. Two thirds (66%) reported resource depletion, and 30% had income below 300 USD a month. Average CD4 count was 416 cells/mm^3 (SD 285). No significant association was identified between either resource depletion or low-income and HIV severity (adjusted mean difference in CD4 count for resource depletion: - 4.16, 95% CI - 82.93, 74.62; adjusted mean difference in CD4 count for low-income: 68.13, 95% CI - 15.78, 152.04). Below-average income and running out of resources were common among PWH who inject drugs and are not on ART in St. Petersburg, Russia. Resource depletion and low-income were not significantly associated with HIV disease severity as captured by CD4 count. The nuanced relationship between socioeconomic status and HIV severity among people with HIV who inject drugs and not on ART merits further examination in a larger sample.

Alcohol-associated liver disease and behavioral and medical cofactors: unmet needs and opportunities. *Front Public Health*. 2024 Apr 4;12:1322460. PMCID: PMC11024463.
Monnig MA, Treloar Padovano H, **Monti PM**.

Chronic liver disease is a leading cause of death in the US and is often preventable. Rising burden, cost, and fatality due to liver disease are driven by intensified alcohol use in the US population and the contributions of comorbid conditions. This mini-review focuses on the topic of liver health in the context of chronic, behavioral cofactors of disease, using

research-based examples from the Brown University Center for Addiction and Disease Risk Exacerbation (CADRE). Our aim is to illustrate the current challenges and opportunities in clinical research addressing liver health in the context of behavioral and medical comorbidity and to highlight next steps in this crucial area of public health research and clinical care.

Comparative costs and potential affordability of a multifaceted intervention to improve treatment outcomes among people with HIV who inject drugs in Russia: economic evaluation of the LINC-II randomized controlled trial. *J Int AIDS Soc*. 2024 Feb;27(2):e26208. PMCID: PMC10895073.
Rosen S, Blokhina E, Truong V, Bereznicka A, Gnatienko N, Quinn E, Lioznov D, Krupitsky E, Michals A, **Lunze K**, **Samet JH**.

Introduction: The LINC-II randomized controlled trial in St. Petersburg, Russia for HIV-positive adults who inject drugs found that a multi-component intervention including initiation of antiretroviral therapy (ART) during admission to an addiction hospital, strengths-based case management and naltrexone significantly increased 12-month HIV viral suppression and ART retention. We conducted a comparative cost analysis to determine if the 12-month cost of the intervention is affordable within the current Russian health system.
Methods: We used LINC-II trial records and questionnaire responses to calculate the resources utilized by each participant in the study, including inpatient days, medications, laboratory tests, outpatient consultations, case manager interactions and opioid medication treatment. Quantities of resources utilized were multiplied by unit costs for each resource estimated from the service fee or price lists used by the study facilities for each specific service delivered. We report the average cost/study primary (viral suppression at 12 months) or secondary (retention in care at 12 months) outcome/participant in 2021 USD and compare costs between study arms.
Results: The trial enrolled 225 participants (111 intervention, 114 control) between September 2018 and December 2020. Viral suppression, non-suppression and missing suppression results were 28% and 14%, 49% and 37%, and 31% and 41% for the control and intervention arms, respectively. Retention results were 35% and 51% for the control and intervention arms, respectively. The average cost per study participant was $2714 in the control arm and $4342 in the intervention arm. The average cost per participant virally suppressed at 12 months was $3662 (control) and $6355 (intervention). The average cost per participant retained at 12 months was $4050 (control) and $5448 (intervention). For those retained, the cost difference between the arms was comprised of opioid treatment (35%), case management (31%), outpatient visits (18%) and additional days of ART (12%).
Conclusions: The LINC-II intervention increased the cost of care for HIV-positive people who inject drugs in Russia significantly, but some components of the intervention, particularly earlier initiation of ART and case management, may be justifiable due to their success in reaching a challenging subgroup of the population in need.

Longitudinal analysis of overlapping psychosocial factors predicting incident hospitalization among mixed HIV serostatus men who have sex with men in the multicenter AIDS cohort study. *AIDS Behav*. 2024 May 4. Epub ahead of print.
Qian Y, Detels R, Comulada WS, Hidalgo MA, Lee SJ, **Biello KB**, Yonko EA, Friedman MR, Palella FJ, Plankey MW, Mimiaga MJ.

Men who have sex with men (MSM) are at increased risk for certain types of chronic diseases and mental health problems. Despite having extended survival in the highly active antiretroviral therapy (HAART) era, MSM living with HIV contend with aging-related diseases and complications with treatment. Consequent hospitalizations incur high costs, fear, low quality of life, and frailty. Unlike heterosexual men, MSM experience more structural violence and "syndemics" of psychosocial factors that not only accelerate HIV acquisition and transmission risk but also may increase morbidity, leading to greater rates of hospitalization. We aim to examine the impact of "syndemic" psychosocial factors on the incidence of hospitalization among geographically diverse MSM in the US. Participants were 1760 MSM from the Multicenter AIDS Cohort Study (MACS) between 2004 and 2019. We examined the relationship between six psychosocial factors (depression,

stimulant use, smoking, heroin use, childhood sexual abuse, and intimate partner violence) and incident hospitalization (admission to a hospital for treatment). We found a positive dose-response relationship between the number of syndemic factors and hospitalization. MSM reporting five or more syndemic factors had over twice the risk of hospitalization compared to MSM without syndemic factors [aRR = 2.14 (95% CI = 1.56, 2.94)]. Psychosocial factors synergistically increased hospitalizations over time. The positive dose-response relationship between the number of syndemic factors and hospitalization and the synergistic effects of these factors underscore the need for interventions that disentangle the syndemics to reduce hospitalization and related costs and improve the quality of life among MSM.

The association of prescribed opioids and incident cardiovascular disease. *J Pain*. 2024 May;25(5):104436. PMCID: PMC11058015.
Sung ML, Eden SK, Becker WC, Crystal S, Duncan MS, Gordon KS, Kerns RD, Kundu S, Freiberg M, **So-Armah KA**, Edelman EJ.

Opioid prescribing remains common despite known overdose-related harms. Less is known about links to nonoverdose morbidity. We determined the association between prescribed opioid receipt with incident cardiovascular disease (CVD) using data from the Veterans Aging Cohort Study, a national prospective cohort of Veterans with/without Human Immunodeficiency Virus (HIV) receiving Veterans Health Administration care. Selected participants had no/minimal prior exposure to prescription opioids, no opioid use disorder, and no severe illness 1 year after the study start date (baseline period). We ascertained prescription opioid exposure over 3 years after the baseline period using outpatient pharmacy fill/refill data. Incident CVD ascertainment began at the end of the prescribed opioid exposure ascertainment period until the first incident CVD event, death, or September 30, 2015. We used adjusted Cox proportional hazards regression models with matching weights using propensity scores for opioid receipt to estimate CVD risk. Among 49,077 patients, 30% received opioids; the median age was 49 years, 97% were male, 49% were Black, and 47% were currently smoking. Prevalence of hypertension, diabetes, current smoking, alcohol and cocaine use disorder, and depression was higher in patients receiving opioids versus those not but were well-balanced by matching weights. Unadjusted CVD incidence rates per 1,000-person-years were higher among those receiving opioids versus those not: 17.4 (95% confidence interval [CI], 16.5-18.3) versus 14.7 (95% CI, 14.2-15.3). In adjusted analyses, those receiving opioids versus those not had an increased hazard of incident CVD (adjusted hazard ratio 1.16 [95% CI, 1.08-1.24]). Prescribed opioids were associated with increased CVD incidence, making opioids a potential modifiable CVD risk factor. PERSPECTIVE: In a propensity score weighted analysis of Veterans Administration data, prescribed opioids compared to no opioids were associated with an increased hazard of incident CVD. Higher opioid doses compared with lower doses were associated with increased hazard of incident CVD. Opioids are a potentially modifiable CVD risk factor.

Pilot RCT comparing low-dose naltrexone, gabapentin and placebo to reduce pain among people with HIV with alcohol problems. *PLoS One*. 2024 Feb 26;19(2):e0297948. PMCID: PMC10896547.
Tsui JI, Rossi SL, Cheng DM, Bendiks S, Vetrova M, Blokhina E, Winter M, Gnatienko N, Backonja M, Bryant K, Krupitsky E, **Samet JH**.

Background: To estimate the effects on pain of two medications (low-dose naltrexone and gabapentin) compared to placebo among people with HIV (PWH) with heavy alcohol use and chronic pain.
Methods: We conducted a pilot, randomized, double-blinded, 3-arm study of PWH with chronic pain and past-year heavy alcohol use in 2021. Participants were recruited in St. Petersburg, Russia, and randomized to receive daily low-dose naltrexone (4.5mg), gabapentin (up to 1800mg), or placebo. The two primary outcomes were change in self-reported pain severity and pain interference measured with the Brief Pain Inventory from baseline to 8 weeks.
Results: Participants (N = 45, 15 in each arm) had the following baseline characteristics: 64% male; age 41 years (SD±7); mean 2 (SD±4) heavy drinking days in the past month and mean pain severity and interference were 3.2 (SD±1) and 3.0 (SD±2), respectively.

Pain severity decreased for all three arms. Mean differences in change in pain severity for gabapentin vs. placebo, and naltrexone vs. placebo were -0.27 (95% confidence interval [CI] -1.76, 1.23; p = 0.73) and 0.88 (95% CI -0.7, 2.46; p = 0.55), respectively. Pain interference decreased for all three arms. Mean differences in change in pain interference for gabapentin vs. placebo, and naltrexone vs. placebo was 0.16 (95% CI -1.38, 1.71; p = 0.83) and 0.40 (95% CI -1.18, 1.99; p = 0.83), respectively.
Conclusion: Neither gabapentin nor low-dose naltrexone appeared to improve pain more than placebo among PWH with chronic pain and past-year heavy alcohol use.