



## CFAR Substance Use Research Core (SURC) Faculty Publication Digest

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

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### Systematic Review of HIV Treatment Adherence Research Among People Who Inject Drugs in the United States and Canada: Evidence To Inform Pre-Exposure Prophylaxis (PrEP) Adherence Interventions

[Bazzi AR, Drainoni ML, Biancarelli DL, Hartman JJ, Mimiaga MJ, Mayer KH & Biello KB. BMC Public Health. 2019;19:31. PMID: PMC6323713.](#)

#### BACKGROUND:

People who inject drugs (PWID) are at increased risk for HIV acquisition and could benefit from antiretroviral pre-exposure prophylaxis (PrEP). However, PrEP has been underutilized in this population, and PrEP adherence intervention needs are understudied.

#### METHODS:

To inform PrEP intervention development, we reviewed evidence on antiretroviral therapy (ART) adherence among HIV-infected PWID. Guided by a behavioral model of healthcare utilization and using the PICOS framework, we conducted a systematic review in four electronic databases to identify original research studies of ART adherence in HIV-infected PWID in the United States and Canada between Jan 1, 2006-Dec 31, 2016. We synthesized and interpreted findings related to developing recommendations for PrEP adherence interventions for PWID.

#### RESULTS:

After excluding 618 duplicates and screening 1049 unique records, we retained 20 studies of PWID (mean n = 465) with adherence-related outcomes (via pharmacy records: n = 9; self-report: n = 8; biological markers: n = 5; electronic monitoring: n = 2). Predisposing factors (patient-level barriers to adherence) included younger age, female sex, and structural vulnerability (e.g., incarceration, homelessness). Enabling resources (i.e., facilitators) that could be leveraged or promoted by interventions included self-efficacy, substance use treatment, and high-quality patient-provider relationships. Competing needs that require specific intervention strategies or adaptations included markers of poor physical health, mental health comorbidities (e.g., depression), and engagement in transactional sex.

#### CONCLUSIONS:

HIV treatment adherence research carries important lessons for efforts to optimize PrEP adherence among PWID. Despite limitations, this systematic review suggests that strategies are needed to engage highly vulnerable and marginalized sub-groups of this underserved population (e.g., younger PWID, women who inject drugs) in PrEP adherence-related research and programming.

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## A Missing Perspective: Injectable Pre-Exposure Prophylaxis for People Who Inject Drugs

[Biello KB, Edeza A, Salhaney P, Biancarelli DL, Mimiaga MJ, Drainoni ML, Childs ES & Bazzi AR. \*AIDS Care\*. 2019; 1-7.](#)

The efficacy of pre-exposure prophylaxis (PrEP) for HIV prevention has been established among people who inject drugs (PWID). HIV uninfected, at risk PWID, could likely benefit from long-acting injectable formulations of PrEP ("LAI-PrEP"); however, its acceptability in this population has not been previously documented. Thirty-three HIV-uninfected PWID in the U.S. Northeast completed an in-depth interview regarding perceived acceptability of LAI-PrEP. Coded data were synthesized using deductive thematic analysis. The majority of PWID interviewed believed LAI-PrEP would be acceptable. Participants perceived that receiving injections every two months would reduce barriers to daily oral PrEP adherence, including forgetting while "high" and safeguarding pills when homeless. A few participants expressed concerns regarding LAI-PrEP, including medical mistrust, a concern that injections could alter their "high" or be "triggering" for PWID. LAI-PrEP has the potential to reduce HIV among PWID; however, their perspectives are largely absent from research examining its efficacy, representing a missed opportunity.

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## Heavy Alcohol Use and Age Effects on HIV-Associated Neurocognitive Function

[Cohen RA, Gullett JM, Porges EC, Woods AJ, Lamb DG, Bryant VE, McAdams M, Tashima K, Cook R, Bryant K, Monnig M, Kahler CW & Monti PM. \*Alcohol Clin Exp Res\*. 2019;43\(1\):147-157.](#)

### BACKGROUND:

There is growing concern about the health impact of heavy alcohol use in people infected with human immunodeficiency virus (HIV+). Mixed findings of past studies regarding the cognitive impact of alcohol use in HIV+ adults have been mixed, with inconsistent evidence that alcohol consumption exacerbates HIV-associated brain dysfunction. This study examined contributions of current heavy drinking, lifetime alcohol use disorder (AUD), and age to cognitive deficits in HIV+ adults, and relative to other HIV-associated clinical factors.

### METHODS:

Cognitive performance of HIV+ adults (n = 104) was assessed, and comparisons were made between heavy current to nonheavy drinkers (NIAAA criteria), lifetime AUD versus no-AUD, and older (>50 years) versus younger participants. Hierarchical regression analyses were conducted to examine the association between cognitive performance and current heavy drinking, lifetime AUD, and older age, while also correcting for HIV clinical factors and history of other substance use.

### RESULTS:

Individuals reporting current heavy drinking and meeting criteria for lifetime AUD demonstrated the greatest degree of deficits across multiple cognitive domains. Deficits were greatest among HIV+ adults with lifetime AUD, and older age was also associated with weaker cognitive performance. Lifetime AUD and older age independently exhibited stronger associations with cognitive performance than HIV clinical factors (e.g., viral load, current CD4, and nadir CD4) or past opiate and cocaine use.

### CONCLUSIONS:

Current heavy drinking and lifetime AUD adversely affect cognitive function in HIV+ adults. Greatest deficits existed when there was a history of AUD and continued current heavy drinking, indicating that past AUD continues to have an adverse impact and should not be ignored. That alcohol use was more strongly associated with cognitive performance than HIV clinical factors underscore clinical importance of targeting reduction in heavy alcohol consumption in HIV+ adults.

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## Chronic Opioid Therapy in People Living With Human Immunodeficiency Virus: Patients' Perspectives on Risks, Monitoring, and Guidelines

[Colasanti J, Lira MC, Cheng DM, Liebschutz JM, Tsui JI, Forman LS, Sullivan M, Walley AY, Bridgen C, Root C, Podolsky M, Abrams K, Harris CE, Armstrong WS, Samet JH & Del Rio C. \*Clin Infect Dis\*. 2019;68\(7\):291-297.](#)

### BACKGROUND:

Chronic opioid therapy (COT) is common in people living with human immunodeficiency virus (PLHIV), but is not well studied. We assessed opioid risk behaviors, perceptions of risk, opioid monitoring, and associated Current Opioid Misuse Measure (COMM) scores of PLHIV on COT.

### METHODS:

COT was defined as  $\geq 3$  opioid prescriptions  $\geq 21$  days apart in the past 6 months. Demographics, substance use, COMM score, and perceptions of and satisfaction with COT monitoring were assessed among PLHIV on COT from 2 HIV clinics.

#### **RESULTS:**

Among participants (N = 165) on COT, 66% were male and 72% were black, with a median age of 55 (standard deviation, 8) years. Alcohol and drug use disorders were present in 17% and 19%, respectively. In 43%, the COMM score, a measure of potential opioid misuse, was high. Thirty percent had an opioid treatment agreement, 66% a urine drug test (UDT), and 12% a pill count. Ninety percent acknowledged opioids' addictive potential. Median (interquartile range) satisfaction levels (1-10 [10 = highest]) were 10 (7-10) for opioid treatment agreements, 9.5 (6-10) for pill counts, and 10 (8-10) for UDT. No association was found between higher COMM score and receipt of or satisfaction with COT monitoring.

#### **CONCLUSIONS:**

Among PLHIV on COT, opioid misuse and awareness of the addictive potential of COT are common, yet COT monitoring practices were not guideline concordant. Patients who received monitoring practices reported high satisfaction. Patient attitudes suggest high acceptance of guideline concordant care for PLHIV on COT when it occurs.

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## **Association of Prescribed Opioids with Increased Risk of Community-Acquired Pneumonia Among Patients With and Without HIV**

[Edelman EJ, Gordon KS, Crothers K, Akgün K, Bryant KJ, Becker WC, Gaither JR, Gibert CL, Gordon AJ, Marshall BDL, Barradas MC, Samet JH, Justice AC, Tate JP & Fiellin DA. \*JAMA Intern Med.\* 2019.](#)

#### **IMPORTANCE:**

Some opioids are known immunosuppressants; however, the association of prescribed opioids with clinically relevant immune-related outcomes is understudied, especially among people living with HIV.

#### **OBJECTIVE:**

To assess the association of prescribed opioids with community-acquired pneumonia (CAP) by opioid properties and HIV status.

#### **DESIGN, SETTING, AND PARTICIPANTS:**

This nested case-control study used data from patients in the Veterans Aging Cohort Study (VACS) from January 1, 2000, through December 31, 2012. Participants in VACS included patients living with and without HIV who received care in Veterans Health Administration (VA) medical centers across the United States. Patients with CAP requiring hospitalization (n = 4246) were matched 1:5 with control individuals without CAP (n = 21 146) by age, sex, race/ethnicity, length of observation, and HIV status. Data were analyzed from March 15, 2017, through August 8, 2018.

#### **EXPOSURES:**

Prescribed opioid exposure during the 12 months before the index date was characterized by a composite variable based on timing (none, past, or current); low (<20 mg), medium (20-50 mg), or high (>50 mg) median morphine equivalent daily dose; and opioid immunosuppressive properties (yes vs unknown or no).

#### **MAIN OUTCOME AND MEASURE:**

CAP requiring hospitalization based on VA and Centers for Medicare & Medicaid data.

#### **RESULTS:**

Among the 25 392 VACS participants (98.9% male; mean [SD] age, 55 [10] years), current medium doses of opioids with unknown or no immunosuppressive properties (adjusted odds ratio [AOR], 1.35; 95% CI, 1.13-1.62) and immunosuppressive properties (AOR, 2.07; 95% CI, 1.50-2.86) and current high doses of opioids with unknown or no immunosuppressive properties (AOR, 2.07; 95% CI, 1.50-2.86) and immunosuppressive properties (AOR, 3.18; 95% CI, 2.44-4.14) were associated with the greatest CAP risk compared with no prescribed opioids or any past prescribed opioid with no immunosuppressive (AOR, 1.24; 95% CI, 1.09-1.40) and immunosuppressive properties (AOR, 1.42; 95% CI, 1.21-1.67), especially with current receipt of immunosuppressive opioids. In stratified analyses, CAP risk was consistently greater among people living with HIV with current prescribed opioids, especially when prescribed immunosuppressive opioids (eg, AORs for current immunosuppressive opioids with medium dose, 1.76 [95% CI, 1.20-2.57] vs 2.33 [95% CI, 1.60-3.40]).

#### **CONCLUSIONS AND RELEVANCE:**

Prescribed opioids, especially higher-dose and immunosuppressive opioids, are associated with increased CAP risk among persons with and without HIV.

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## **Positive Strategies To Enhance Problem-Solving Skills (STEPS): A Pilot Randomized, Controlled Trial of a Multicomponent, Technology-Enhanced, Customizable Antiretroviral Adherence Intervention for HIV-Infected Adolescents and Young Adults**

[Mimiaga MJ, Bogart LM, Thurston IB, Santostefano CM, Closson EF, Skeer MR, Biello KB & Safren SA. \*AIDS Patient Care STDS\*. 2019;33\(1\):21-24.](#)

Adolescents are disproportionately impacted by HIV in the United States. Optimal effects from antiretroviral therapy (ART) can be achieved through stringent adherence to a daily medication regimen; for adolescents, this may be interrupted due to complex barriers unique to this age group. We previously conducted formative qualitative interviews with HIV-infected adolescents to identify key barriers facing adolescents regarding ART adherence and potential strategies to address these barriers. These data were used to inform an ART adherence intervention designed to overcome difficulties unique to HIV-infected adolescents (e.g., internalized stigma and HIV-related shame, disclosure to sexual partners, social life, and extracurricular activities at school, etc.). The resulting intervention-"Positive Strategies To Enhance Problem-solving Skills (Positive STEPS)"-combines five individual counseling sessions with daily text message reminders. We conducted a pilot randomized controlled trial of the intervention against a standard of care control and report on the feasibility of procedures and participant acceptability of the intervention in terms of content, structure, and format. ART adherence was measured in both arms through Medication Event Monitoring System pill caps and self-report. Feasibility and acceptability of the Positive STEPS intervention was evidenced by 90% retention for the intervention sessions; 100% completion of the four-month assessment; and positive responses on postintervention evaluation forms (all intervention participants rated Positive STEPS as "acceptable" or "very acceptable") and brief exit interviews. At the 4-month assessment visit, the change in ART adherence among the intervention group [mean change score = 13%, standard deviation (SD) = 29.5] was significantly higher compared with the standard of care group (mean change score = -26%, SD = 26.0; Cohen's *d* effect size = 1.43, confidence interval = 0.17-2.49, *p* = 0.02). Future testing of the intervention in a fully powered randomized controlled trial to determine efficacy is warranted.

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## **A Randomized Pilot Study of a Group-Delivered HIV Risk Reduction Intervention for At-Risk Urban Men Who Have Sex with Men Who Regularly Attend Private Sex Events**

[Mimiaga MJ, Hughto JMW & Reisner. SL. \*Arch Sex Behav\*. 2019.](#)

Across HIV prevention studies, as many as 25% of men who have sex with men (MSM) report meeting male partners at private sex events and attendance is associated with increased number of sexual partners, condomless anal sex (CAS), and HIV infection. Despite the need for effective HIV prevention interventions, no risk reduction interventions have been tested to reduce HIV sexual risk of MSM that regularly engage in sexual risk at private sex events. This randomized pilot study assessed the feasibility and acceptability of an HIV risk reduction intervention to reduce CAS among urban MSM (N = 14) reporting risk at a private sex event in the prior 12 months. The intervention arm received four group sessions (2 h/session) focusing on HIV risk reduction education and skills building. Both the intervention (n = 8) and control (n = 6) conditions received HIV testing and pre- and posttest risk reduction counseling and completed a sexual risk and psychosocial assessment visit at baseline and 3 months post-intervention. In addition, intervention participants completed a brief exit interview post-intervention. Mean age was 37 years, and 57% were racial/ethnic minorities. At follow-up, the intervention group reported greater reductions in sexual risk behavior in the past 3 months including number of CAS episodes, number of partners at private sex events, and CAS episodes at private sex events. The intervention group also reported reduced sexual compulsivity, increases in HIV disclosure, and reduced drug use at private sex events over study follow-up. Exit interviews revealed that participants found the intervention to be highly acceptable. Findings demonstrate feasibility of procedures, participant acceptability, and initial promise of a group-delivered HIV risk reduction intervention for MSM who attend and engage in CAS at private sex events. Further testing of this intervention in a larger pilot randomized controlled trial is warranted.

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## **Elimination of HIV Transmission Through Novel and Established Prevention Strategies Among People Who Inject Drugs**

[Reddon H, Marshall BDL & Milloy MJ. \*Lancet HIV\*. 2019;6\(2\):128-136.](#)

Despite the effectiveness of existing HIV prevention strategies for people who inject drugs (PWID), uncontrolled outbreaks of HIV among this group are common and occur around the world. In this Review, we summarise recent evidence for novel and established HIV prevention approaches to eliminate HIV transmission among PWID. Effective HIV prevention strategies include mobile needle and syringe programmes, pre-exposure prophylaxis, supervised injection facilities, and, to a lesser extent, some behavioural interventions. Studies have also shown the cost-effectiveness of long-standing HIV prevention strategies including needle and syringe programmes, opioid agonist therapy, and antiretroviral therapy for prevention. Although each individual intervention can reduce the risk of HIV acquisition among PWID, there is a consensus that a combination of approaches is required to achieve substantial and durable reductions in HIV transmission. Unfortunately, in many settings, the implementation of these interventions is often limited by public and political opposition that manifests as structural barriers to HIV prevention, such as the criminalisation of drug use. Given that there is ample evidence showing the effectiveness of several HIV prevention methods, social and political advocacy will be needed to overcome these barriers and integrate innovative HIV prevention approaches with addiction science to create effective drug policies.

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## **Provider Opioid Prescribing Practices and the Belief That Opioids Keep People Living With HIV Engaged in Care: A Cross-Sectional Study**

[Tsui JI, Walley AY, Cheng DM, Lira MC, Liebschutz JM, Forman LS, Sullivan MM, Colasanti J, Root C, O'Connor K, Shanahan CW, Bridden CL, Del Rio C & Samet JH. \*AIDS Care\*. 2019;11:1-5.](#)

We describe HIV providers' opioid prescribing practices and assess whether belief that chronic opioid therapy (COT) keeps people living with HIV (PLWH) engaged in care is associated with differences in these practices among providers from two HIV clinics. We conducted logistic regression to evaluate the association between the belief that COT keeps PLWH engaged in care and at least one component of guideline-recommended care (i.e., urine drug tests, treatment agreements, and/or prescription monitoring program use). The sample included 41 providers with a median age of 42 years, 63% female, 37% non-white. Routine adherence to guideline-recommended practices was: 34% urine drug tests, 27% treatment agreements, and 17% prescription monitoring program. Over half [54%] agreed that COT keeps PLWH engaged in care. There was no significant association between belief that COT keeps PLWH engaged in care and routinely providing any recommended COT care component (aOR 2.38; 95% CI 0.65-8.73). Most HIV providers do not routinely follow guidelines for opioid prescribing. We observed a positive association between belief that COT keeps PLWH engaged in care and following any guideline-recommended prescribing practices, although the result was not statistically significant. Interventions are needed to improve guideline-concordant care for COT by HIV providers.

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## **Causal Effects of Alcohol Intoxication on Sexual Risk Intentions and Condom Negotiation Skills Among High-Risk Men Who Have Sex with Men (MSM)**

[Wray TB, Celio MA, Pérez AE, DiGuseppi GT, Carr DJ, Woods LA & Monti \*PMAIDS Behav\*. 2019;23\(1\):161-174.](#)

Alcohol use is a key risk factor for HIV infection among MSM, in part because intoxication may interfere with the use of prevention methods like condoms. However, few studies have examined whether this is due to alcohol's pharmacological or expectancy effects or explored the specific aspects of sexual decision-making that may be affected. In this study, high-risk, heavy drinking MSM (N = 121) were randomly assigned to receive either (1) alcohol beverages, (2) placebo beverages, or (3) control beverages, before navigating a video-based sexual risk scenario that assessed several aspects of sexual decision-making. Results showed that condom use intentions and negotiation behaviors were lower among alcohol and placebo participants compared with controls, but that few significant differences emerged between the alcohol and placebo groups. These findings contrast with similar past studies, and suggest that alcohol's expectancy effects may play a role in sexual decision-making.

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## **Vulnerable Periods: Characterizing Patterns of Sexual Risk and Substance Use During Lapses in Adherence to HIV Pre-exposure Prophylaxis Among Men Who Have Sex With Men**

[Wray TB, Chan PA, Kahler CW, Simpanen EM, Liu T & Mayer KH. \*JAIDS\*. 2019;80\(3\):276-283.](#)

**BACKGROUND:**



Pre-exposure prophylaxis (PrEP) is highly efficacious, but some groups of men who have sex with men may have difficulty adhering to daily dosing. Prevention-effective adherence suggests that PrEP's efficacy depends on adherence at the time of HIV exposure; yet, few studies have examined how exposures (ie, high-risk sex) overlap with periods of consecutive missed PrEP doses. Substance use may also play a role in these vulnerable periods.

**METHODS:**

We used digital pill bottles to monitor the daily adherence of 40 PrEP-experienced patients recruited from an outpatient clinic in the Northeastern US over a six-month period. Participants also completed detailed online diaries every 2 weeks during this time that surveyed their sexual behavior and substance use each day.

**RESULTS:**

Daily adherence was high overall (M = 83.9%, SD = 18.0%), but 53% (N = 21) had a lapse of > 3 consecutive daily PrEP doses over 6 months. Participants' rate of engaging in high-risk condomless anal sex (CAS) did not differ across lapse days versus continuously adherent days. Alcohol use was not associated with engaging in CAS during a PrEP lapse. However, participants reported engaging in CAS significantly more often during a PrEP adherence lapse on days when they also used stimulant drugs.

**CONCLUSIONS:**

Men who have sex with men may have periodic difficulty adhering to PrEP at the specific times when they are at risk. Stimulant drug use could play an important role in increasing HIV risk specifically during adherence lapses.

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## **A Preliminary Randomized Controlled Trial of Game Plan, A Web Application to Help Men Who Have Sex with Men Reduce Their HIV Risk and Alcohol Use**

[Wray TB, Kahler CW, Simpanen EM & Operario D. \*AIDS Behav.\* 2019.](#)

Alcohol use is a key risk factor for HIV infection among men who have sex with men (MSM). Past studies show that brief motivational interventions (BMI) can increase the use of prevention methods (e.g., condoms), reduce alcohol use, and can be adapted for web-based delivery. However, few studies have explored these interventions' effects in MSM. Forty high-risk, heavy drinking MSM who sought rapid HIV testing were randomly assigned to receive either (1) standard post-test counseling (SPC) alone, or (2) SPC plus Game Plan (GP), a tablet-based BMI for alcohol use and HIV risk. Over three months of follow-up, GP participants reported 24% fewer heavy drinking days, 17% fewer alcohol problems, and 50% fewer new anal sex partners than controls. GP participants also reported fewer high-risk condomless anal sex events than controls, but these differences were not significant. These initial results suggest that web-based BMIs may be promising tools to help MSM reduce health risk behaviors.

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