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CFAR Substance Use Research Core (SURC) Quarterly Digest

New research on HIV and substance use by our SURC faculty, along with other relevant updates.

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

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

Visit the SURC webpage

SURC Updates

PrEP Meeting

The Center for AIDS Research Substance Use Research Core held a PrEP Research Meeting on July 22, 2020. Members and collaborators from the CFAR SURC community presented their projects, highlighting their project's intersection with substance use. Thank you to the approximately 30 collaborators who presented or attended!

Keep an eye out for information about our next PrEP meeting, which will be taking place in early Fall. To see slides from our meeting in July, information on presenters and their projects, and other related resources, see the PrEP meeting Google Drive linked here.

COBRE Grants

Please see linked here a call for COBRE pilots that address stigma. If you or someone you know is applying for one of these, please contact Natalia Gnatienko (natalia.gnatienko@bmc.org) as we have stigma expertise within our group and would be excited to support submissions in response to this announcement. Letters of Intent are due September 15, 2020, and applications are due no later than 5:00 PM on October 15, 2020.

New Publications

Alcohol use and antiretroviral adherence among patients living with HIV:

is change in alcohol use associated with change in adherence?

Williams EC, McGinnis KA, Rubinsky AD, Matson TE, Bobb JF, Lapham GT, Edelman EJ, Satre DD, Catz SL, Richards JE, Bryant KJ, **Marshall BDL**, Kraemer KL, Crystal S, Gordon AJ, Skanderson M, Fiellin DA, Justice AC, Bradley KA. *AIDS Behav*. 2020;10.1007/s10461-020-02950-x.

Alcohol use increases non-adherence to antiretroviral therapy (ART) among persons living with HIV (PLWH). Dynamic longitudinal associations are understudied. Veterans Aging Cohort Study (VACS) data 2/1/2008-7/31/16 were used to fit linear regression models estimating changes in adherence (% days with ART medication fill) associated with changes in alcohol use based on annual clinically-ascertained AUDIT-C screening scores (range - 12 to + 12, 0 = no change) adjusting for demographics and initial adherence. Among 21,275 PLWH (67,330 observations), most reported no (48%) or low-level (39%) alcohol use initially, with no (55%) or small (39% ≤ 3 points) annual change. Mean initial adherence was 86% (SD 21%), mean annual change was - 3.1% (SD 21%). An inverted V-shaped association was observed: both increases and decreases in AUDIT-C were associated with greater adherence decreases relative to stable scores [$p < 0.001$, $F (4, 21,274)$]. PLWH with dynamic alcohol use (potentially indicative of alcohol use disorder) should be considered for adherence interventions.

An integrated videoconferencing intervention for chronic pain and heavy drinking among patients in HIV-care: a proof-of-concept study.

Palfai TP, **Saitz R**, Kratzer MPL, Taylor JL, Otis JD, Bernstein JA.*AIDS Care*. 2020;1-8.

Chronic pain and heavy drinking are common comorbid conditions among people living with HIV/AIDS (PLWHA). An integrated approach to address these co-occurring conditions in a manner that facilitates treatment utilization would represent an important advance in HIV-care. This study examined the acceptability and feasibility of a tailored, videoconferencing intervention to reduce chronic pain and heavy drinking among PLWHA. Participants in HIV-care (n = 8) completed baseline assessments and an in-person intervention session followed by 6 videoconferencing sessions. Acceptability and feasibility were assessed with patient satisfaction ratings and interview responses 8 weeks following baseline along with videoconferencing use during the intervention period. Treatment satisfaction and comprehensibility ratings were high and supported by interview responses indicating the value of the intervention content, treatment alliance, and format. All participants successfully enabled videoconferencing on their own smartphones and completed a median number of 4.5 (out of 6) video-sessions. Changes in heavy drinking and pain provided additional support for the potential utility of this approach. Results suggest that this videoconferencing intervention is an acceptable and feasible method of addressing chronic pain and heavy drinking among PLWHA. Findings provide the basis for future work to examine the efficacy of this approach in a Stage 1b trial.

Are we missing opioid-related deaths among people with HIV?

Becker WC, Gordon KS, Edelman EJ, Goulet JL, Kerns RD,**Marshall BDL**, Fiellin DA, Justice AC, Tate JP. *Drug Alcohol Depend*. 2020;212:108003.

Background:
Ascertainment of unnatural and overdose death may be unreliable among individuals with life-limiting conditions such as HIV infection. We sought to determine whether the relationship between opioid use and unnatural death differs among decedents with HIV (DWH) and those without.

Methods:
Decedents in the Veterans Aging Cohort Study (VACS) from 2002 to 14 were linked to the National Death Index cause of death file. Deaths were classified as unnatural, overdose (a subset of unnatural), or other. We defined opioid use as self-reported illicit use or receipt of prescribed opioids. Treating unnatural and overdose deaths as outcomes, we calculated odds ratios for opioid exposure by HIV status, with and without adjustment for disease severity using VACS Index.

Results:
Among 561 decedents without HIV (DWOH) and 884 DWH, 11 % and 8 % respectively were classified as unnatural deaths and 4 % and 2 % were classified as overdose deaths. Among DWOH, opioid use was associated with 2-fold greater odds of unnatural (OR 2.3; 95 % CI 1.3-4.0) and 4-fold greater odds of overdose death (OR 4.5; 95 % CI 1.5-13.7); in adjusted analyses, opioid use was associated with unnatural death (OR 2.6; 95 % CI 1.3-4.9) and with overdose (OR 4.2; 95 % CI 1.4-12.7). Opioid use was not associated with unnatural or overdose death among DWH.

Conclusion:
Opioid use was strongly associated with unnatural and overdose death among DWOH but not among DWH suggesting potential differential misclassification. Caution should be used in interpreting prevalence, incidence and risk factors for unnatural and overdose cause of death among patients with life-limiting conditions such as HIV.

Assessing the interaction between depressive symptoms and alcohol use prior to antiretroviral therapy on viral suppression among people living with HIV in rural Uganda.

Foley JD, Sheinfil A, Woolf-King SE, Fatch R, Emenyonu NI, Muyindike WR, Kekibiina A, Ngabirano C, **Samet JH**, Cheng DM, Hahn JA. *AIDS Care*. 2020;1-7.

Although there is evidence of individual associations between depressive symptoms and hazardous alcohol use with suboptimal antiretroviral therapy (ART) adherence among people living with HIV (PLWH), few studies have established how the two risk factors may interact to predict viral suppression. We conducted secondary data analyses with two cohorts of Ugandan PLWH (N = 657) to investigate the hypothesized interaction between depressive symptoms (Center for Epidemiological Studies Depression Scale) and hazardous alcohol use (Alcohol Use Disorder Identification Test -Consumption and/or Phosphatidylethanol biomarker) prior to ART initiation with viral suppression (<550 copies/ml). We were unable to detect an interaction between depressive symptoms and hazardous alcohol use prior to ART initiation with viral suppression in the first two years (M = 19.9 months) after ART initiation (p = 0.75). There was also no evidence of a main effect association for depressive symptoms (Adjusted Odds Ratio [AOR] = 0.88, 95% Confidence Interval [CI]: 0.50, 1.55) or hazardous alcohol use (AOR = 1.37, 95% CI: 0.80, 2.33). PLWH with depressive symptoms and/or hazardous alcohol use appear to exhibit similar levels of viral suppression as others in care; further work is needed to determine effects on HIV testing and treatment engagement.

Design of a randomized controlled trial of smoking cessation medications for alcohol reduction among HIV-positive heavy drinkers and daily smokers in St. Petersburg, Russia.

Tindle H, Freiberg M, **Gnatienko N**, Blokhina E, Cheng D, Yaroslavtseva T, Bendiks S, Winter M, Krupitsky E, **Samet JH**. *Contemp Clin Trials Commun*. 2020;19.

Background:
HIV, heavy drinking, and smoking are all pro-inflammatory and increase risk for coronary heart disease (CHD). Interventions that reduce alcohol use, smoking, or both in HIV-positive people could lower inflammation, CHD and death risk. Varenicline and cytisine are proven therapies for smoking cessation and may also reduce alcohol consumption. The comparative efficacy of varenicline and cytisine to reduce alcohol consumption has not been tested, nor has their comparative effectiveness been reported for smoking.

Objective:
This paper describes the protocol of the Studying Partial agonists for Ethanol and Tobacco Elimination in Russians with HIV (St PETER HIV), a four-arm parallel-group randomized controlled trial comparing effects of varenicline, cytisine, and nicotine replacement therapy (NRT).

Methods:
The study is recruiting four hundred HIV-positive heavy drinking smokers interested in cutting down on alcohol and/or tobacco in St. Petersburg, Russia. Participants are randomly assigned to receive either active varenicline + NRT placebo, varenicline placebo + active NRT, active cytisine + NRT placebo, cytisine placebo + active NRT. All participants receive evidence-based counseling for alcohol and tobacco use, one active medication, and one placebo. Outcomes are: 1) % heavy drinking days in the past month (primary study outcome at three months) and alcohol craving; 2) cigarettes per day (primary smoking outcome at 3 months) and 7-day point prevalence abstinence and; 3) inflammation, CHD risk, and mortality risk.

Conclusion:
St PETER HIV addresses the paucity of randomized controlled trial data to guide treatment of alcohol consumption and smoking in HIV-positive heavy drinking smokers.

Effect of zinc supplementation vs placebo on mortality risk and HIV disease progression among HIV-positive adults with heavy alcohol use: a randomized clinical trial.

Freiberg MS, Cheng DM, **Gnatienko N**, Blokhina E, Coleman SM, Doyle MF, Yaroslavtseva T, Bridden C, **So-Armah K**, Tracy R, Bryant K, Lioznov D, Krupitsky E,**Samet JH**. *JAMA Netw Open*. 2020;3(5):e204330. Published 2020 May 1.

Importance:
Zinc supplementation can reduce alcohol-related microbial translocation and inflammation.

Objective:
To assess whether zinc supplementation reduces markers of mortality and risk of cardiovascular disease, reduces levels of inflammation and microbial translocation, and slows HIV disease progression in people with heavy alcohol use who are living with HIV/AIDS.

Design, setting, and participants:
This study is a double-blinded placebo-controlled randomized clinical trial of zinc supplementation among participants recruited from 2013 to 2015. Participants were recruited from HIV and addiction clinical and nonclinical care sites in St Petersburg, Russia. Participants were adults (aged 18-70 years) with documented HIV infection who were antiretroviral therapy-naive at baseline and had past 30-day heavy alcohol consumption. Data analysis was performed from February 2017 to February 2020.

Intervention:
Pharmacy-grade zinc gluconate supplementation (15 mg for men and 12 mg for women, taken daily by mouth for 18 months) was compared with a placebo.
Main outcomes and measures: The primary outcome was mortality risk measured as a change in Veterans Aging Cohort Study (VACS) Index score between baseline and 18 months. The VACS Index scores range from 0 to 164, with higher scores indicating higher mortality risk. Secondary outcomes were change in CD4 cell count between baseline and 18 months, the assessment of cardiovascular disease risk (Reynolds Risk Score, which ranges from 0% to 100%, with higher scores indicating higher risk), and changes in inflammatory or microbial translocation biomarkers at 18 months. Adjusted linear regression analyses were performed.

Results:
A total of 254 participants (184 men [72%]; mean [SD] age, 34 [6] years) were enrolled in the trial; 126 were randomized to receive zinc, and 128 were randomized to receive placebo. Participants had high CD4 cell counts (mean [SD], 521 [292] cells/mm3), and 188 (74%) reported heavy drinking in the past week. In the main analyses, zinc supplementation did not affect changes in the VACS Index score at 18 months (change for zinc, mean [SD], 0.49 [14.6]; median [interquartile range], 0.0 [-7.0 to 6.0]; change for placebo, mean [SD], 5.5 [17.2]; median [interquartile range], 6.0 [-6.0 to 14.0]; adjusted mean difference [AMD], -4.68; 95% CI, -9.62 to 0.25; P = .06) or any secondary outcomes, including change in CD4 cell count (AMD, 41.8 cells/mm3; 95% CI, -20.3 to 103.8 cells/mm3; P = .19), Reynolds Risk Score (AMD, -0.014; 95% CI, -0.167 to 0.139; P = .85), interleukin-6 level (AMD, -0.13 pg/mL; 95% CI, -0.38 to 0.11 pg/mL; P = .30), dimerized plasmin fragment D level (AMD, -0.21 µg/mL fibrinogen equivalent units; 95% CI, -0.48 to 0.07 µg/mL fibrinogen equivalent units; P = .14), soluble CD14 level (AMD, -38.01 ng/mL; 95% CI, -166.90 to 90.88 ng/mL; P = .56), intestinal fatty acid binding protein level (AMD, 0.08 pg/mL; 95% CI, -0.07 to 0.22 pg/mL; P = .32), and lipopolysaccharide binding protein level (AMD, -0.09 ng/mL; 95% CI, -0.23 to 0.06 ng/mL; P = .24). In the per-protocol analyses, zinc supplementation statistically significantly affected changes in the VACS Index score at 18 months (AMD, -7.49; 95% CI, -13.74 to -1.23; P = .02); however, the adherence rate to zinc supplementation was 51%.

Conclusions and relevance:
Zinc supplementation did not reduce mortality risk, CD4 cell counts, cardiovascular disease risk, and levels of inflammation or microbial translocation in people with heavy alcohol use who are living with HIV/AIDS. Zinc supplementation did not change the VACS Index score but may have been limited by low adherence.

Food insecurity and substance use in people with HIV infection and substance use disorder.

Raja A, Heeren TC, **Walley AY**, Winter MR, Mesic A, **Saitz R**. *Subst Abus.* 2020;1-9.

Background:
Food insecurity and substance use are common among people living with HIV (PLWH). Substance use may help people cope with hunger and thus be associated with food insecurity, but the association is uncertain. This study assessed whether, in PLWH and substance dependence, if there was an association between food insecurity and substance use.

Methods*:*
We studied adults with HIV and current substance dependence or ever injection drug use interviewed at 12 and 24 months after enrollment in a prospective cohort study. The presence of food insecurity (insufficient food quantity or quality, or anxiety about its availability) was assessed using the Household Food Insecurity Assessment Scale questionnaire (HFIAS). Unhealthy alcohol use was assessed with the Alcohol Use Disorder Identification Test - Consumption (AUDIT-C) and past 30-day other drug use with the Addiction Severity Index. Associations using repeat cross-sectional data from each of two time-points, 12 months apart, from the same participants were tested using generalized estimating equations logistic regressions.

Results:
The 233 participants had a mean age of 50 years and 65% were male. At the first interview, 44% reported food insecurity, 40% unhealthy alcohol use, 25% past 30-day cocaine use, and 17% past 30-day illicit

opioid use. In analyses adjusted for demographics, social factors, physical and mental health function, and substance use related variables, there was no significant association between food insecurity and unhealthy alcohol use (adjusted odds ratio (aOR) = 1.06 (95% CI: 0.59, 1.87)). Those with food insecurity had higher odds of illicit opioid use (aOR = 2.5 (95% CI: 1.12, 5.58)) and cocaine use (aOR = 1.95 (CI 95%: 1.00, 3.81)).

Conclusion:
Food insecurity was not associated with unhealthy alcohol use but was associated with cocaine and illicit opioid use. Given the prevalence and impact substance use has on PLWH, food insecurity should be identified and addressed.

Improving the delivery of chronic opioid therapy among people living with HIV: a cluster randomized clinical trial.

Samet JH, Tsui JI, Cheng DM, Liebschutz JM, Lira MC,**Walley AY**, Colasanti JA, Forman LS, Root C, Shanahan CW, Sullivan MM, Bridden CL, Abrams C, Harris C, Outlaw K, Armstrong WS, Del Rio C. *Clin Infect Dis*. 2020;ciaa1025.

Background:
Chronic pain is prevalent among people living with HIV (PLWH); managing pain with chronic opioid therapy (COT) is common. HIV providers often diverge from prescribing guidelines.

Methods:
This two-arm, unblinded cluster-randomized clinical trial assessed whether the Targeting Effective Analgesia in Clinics for HIV (TEACH) intervention improves guideline-concordant care compared to usual care for PLWH on COT. The trial was implemented from 2015-2018 with 12-month follow-up at safety-net hospital-based HIV clinics in Boston and Atlanta. We enrolled 41 providers and their 187 patients on COT. Prescribers were randomized 1:1 to either a 12-month intervention consisting of a nurse care manager with an interactive electronic registry, opioid education, academic detailing and access to addiction specialists or a control condition consisting of usual care. Two primary outcomes were assessed through electronic medical records: ≥2 urine drug tests and any early COT refills by 12 months. Other outcomes included possible adverse consequences.

Results:
At 12-months, the TEACH intervention arm had higher odds of ≥2 urine drug tests than the usual care arm (71% vs. 20%, adjusted odds ratio [AOR]: 13.38; 95% confidence interval [CI]: 5.85-30.60; p<0.0001). We did not detect a statistically significant difference in early refills (22% vs. 30%; AOR: 0.55; 95% CI: 0.26-1.15; p=0.11), pain severity (6.30 vs. 5.76; adjusted mean difference 0.10; 95% CI: -1.56-1.75; p=0.91), or HIV viral load suppression (86.9% vs. 82.1%; AOR: 1.21; 95% CI: 0.47-3.09; p=0.69).

Conclusions:
TEACH is a promising intervention to improve adherence to COT guidelines without evident adverse consequences.

Motivation to quit drinking in individuals coinfected with HIV and hepatitis C.

Hayaki J, Anderson BJ, Herman DS, Moitra E, Pinkston MM, Kim HN,**Stein MD**. *AIDS Behav.* 2020;24(6):1709-1716.

Alcohol consumption is common among individuals coinfected with HIV and hepatitis C (HCV) despite the uniquely harmful effects in this population. Limited research has examined factors that could influence drinking reduction or cessation among HIV/HCV coinfected persons; this study investigates motivation to quit. Participants were 110 alcohol-consuming HIV/HCV coinfected patients recruited from medical clinics. Participants self-reported 90-day drinking frequency and intensity; alcohol-related problems; reasons to quit drinking; reasons to drink; and motivation to quit drinking. Participants consumed alcohol on 54.1 (± 26.9) of the past 90 days. In a multivariate model that controlled for demographic variables, motivation to quit drinking was directly associated with alcohol-related problems ($\beta_{y \cdot x}$ = 0.35, p = .007) and reasons to quit drinking ($\beta_{y \cdot x}$ = 0.23, p = .021), and inversely associated with drinking for enhancement ($\beta_{y \cdot x}$ = -0.36, p = .004). This study identified several factors associated with motivation to quit drinking in a sample of alcohol-consuming HIV/HCV patients.

Predictors of pain-related functional impairment among people living with HIV on long-term opioid therapy.

Serota DP, Capozzi C, Lodi S, Colasanti JA, Forman LS, Tsui JI,**Walley AY**, Lira MC, **Samet J**, Del Rio C, Merlin JS. *AIDS Care*. 2020;1-9.

People living with HIV (PLWH) have high levels of functional impairment due to pain, also called pain interference. Long-term opioid therapy (LTOT) is commonly prescribed for chronic pain among PLWH. We sought to better understand the predictors of pain interference, measured with the Brief Pain Inventory Interference subscale (BPI-I), among PLWH with chronic pain on LTOT. Using a prospective cohort of PLWH on LTOT we developed a model to identify predictors of increased pain interference over 1 year of follow up. Participants (*n* = 166) were 34% female, 72% African American with a median age of 55 years, and 40% had severe pain interference (BPI-I ≥ 7). In multivariable models, substance use disorder, depressive symptoms, PTSD symptoms, financial instability, and higher opioid doses were associated with increased pain interference. Measures of behavioral health and socioeconomic status had the most consistent association with pain interference. In contrast, the biomedical aspects of chronic pain and LTOT - comorbidities, duration of pain - were not predictive of pain interference. PLWH with chronic pain on LTOT with lower socioeconomic status and behavioral health symptoms have higher risk of pain interference. Addressing the social determinants of health and providing access to behavioral health services could improve patients' pain-related functional status.

Real-world eligibility for HIV pre-exposure prophylaxis among people who inject drugs.

Picard J, **Jacka B**, Høj S, Laverdière É, Cox J, Roy É, Bruneau J*AIDS Behav.* *AIDS Behav.* 2020;24(8):2400-2408.

Recent studies have highlighted the efficacy of and willingness to use pre-exposure prophylaxis (PrEP) to prevent HIV infection among people who inject drugs (PWID), however knowledge of real-world applicability is limited. We aimed to quantify the real-world eligibility for HIV-PrEP among HIV-negative PWID in Montreal, Canada (n = 718). Eligibility was calculated according to US Centers for Disease Control and Prevention (CDC) guidelines and compared to risk of HIV acquisition according to the assessing the risk of contracting HIV (ARCH-IDU) risk screening tool. Over one-third of participants (37%) were eligible for HIV PrEP, with 1/3 of these eligible due to sexual risk alone. Half of participants were considered high risk of HIV acquisition according to ARCH-IDU, but there was poor agreement between the two measures. Although a large proportion of PWID were eligible for HIV-PrEP, better tools that are context- and location-informed are needed to identify PWID at higher risk of HIV acquisition.

Stigma and quality of co-located care for HIV-positive people in addiction treatment in Ukraine: a cross-sectional study.

Sereda Y, Kiriazova T, Makarenko O, Carroll J, Rybak N, Chybisov A, Bendiks S, Idrisov B, Dutta A, Gillani FS, **Samet JH**, Flanigan T, **Lunze K**. *J Int AIDS Soc.* 2020;23(5):e25492.

Introduction:
Co-located treatment for HIV and opioid use disorder has been shown to improve care outcomes for HIV-positive people who inject drugs (PWID) in Ukraine. However, patients continue to be stigmatized for both HIV and substance use. This study aimed to assess whether co-located care for HIV-positive PWID receiving opioid agonist treatment (OAT) services in Ukraine is associated with less stigma and better perceived quality of HIV services.

Methods:
This cross-sectional study enrolled 191 HIV-positive PWID who received OAT services at three healthcare facilities providing substance use treatment (OAT only) and at four facilities that provided co-located care (both OAT and HIV treatment) in six regions in Ukraine during July-September, 2017. Primary outcomes were HIV stigma (Berger scale), substance use stigma (Substance Abuse Stigma Scale) and intersectional stigma (both stigma forms above 75th percentile). Secondary outcome was quality of HIV care, a composite score based on a package of received services. Linear and ordinal regressions were used to assess the predictors of selected outcomes.

Results:
Study participants were 75% male, mean age 40 ± 7 years; 47% received co-located care, and 10.5% had both high HIV and substance use stigma. Co-located care was neither associated with HIV nor substance use stigma but it was linked to better quality of HIV care (adjusted odds ratio: 4.13; 95% CI: 2.31, 7.54). HIV stigma was associated with suicide attempts (adjusted beta (aβ): 5.90; 95% CI: 2.05, 9.75), and substance use stigma was linked to poor mental health (aβ: -0.26; 95% CI: -0.44, -0.08) and lower likelihood of receipt of services from non-governmental organization (NGO; aβ: -6.40; 95% CI: -10.23, -2.57).

Conclusion:
One in ten people with HIV in this cohort who received OAT services experienced high levels of both HIV and substance use stigma, which was associated with poorer mental health and less NGO support. Co-located HIV and OAT services were linked to better perceived quality of HIV care, but did not seem to reduce stigma for this key population. Stigma interventions for PWID, possibly delivered involving NGOs, may be an approach to mitigate this challenge.

Trajectories of self-reported opioid use among patients with HIV engaged in care: results from a national cohort study.

Edelman EJ, Li Y, Barry D, Brennan Braden J, Crystal S, Kerns RD, Gaither JR, Gordon KS, Manhapra A, Merlin JS, Moore BA, Oldfield BJ, Park LS, Rentsch CT, Skanderson M, Williams EC, Justice AC, Tate JP, Becker WC, **Marshall BDL**. *J Acquir Immune Defic Syndr.* 2020;84(1):26-36.

Background:
No prior studies have characterized long-term patterns of opioid use regardless of source or reason for use among patients with HIV (PWH). We sought to identify trajectories of self-reported opioid use and their correlates among a national sample of PWH engaged in care.
Setting: Veterans Aging Cohort Study, a prospective cohort including PWH receiving care at 8 US Veterans Health Administration (VA) sites.

Methods:
Between 2002 and 2018, we assessed past year opioid use frequency based on self-reported "prescription painkillers" and/or heroin use at baseline and follow-up. We used group-based trajectory models to identify opioid use trajectories and multinomial logistic regression to determine baseline factors independently associated with escalating opioid use compared to stable, infrequent use.

Results:
Among 3702 PWH, we identified 4 opioid use trajectories: (1) no lifetime use (25%); (2) stable, infrequent use (58%); (3) escalating use (7%); and (4) de-escalating use (11%). In bivariate analysis, anxiety; pain interference; prescribed opioids, benzodiazepines and gabapentinoids; and marijuana use were associated with escalating opioid group membership compared to stable, infrequent use. In multivariable analysis, illness severity, pain interference, receipt of prescribed benzodiazepine medications, and marijuana use were associated with escalating opioid group membership compared to stable, infrequent use.

Conclusion:
Among PWH engaged in VA care, 1 in 15 reported escalating opioid use. Future research is needed to understand the impact of psychoactive medications and marijuana use on opioid use and whether enhanced uptake of evidence-based treatment of pain and psychiatric symptoms can prevent escalating use among PWH.