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ABSTRACT BOOK

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ORAL COMMUNICATION: ADVANCES IN CONTINGENCY MANAGEMENT

NON-TREATMENT SEEKING ADOLESCENTS SHOW A REDUCTION IN CANNABIS USE FOLLOWING 30 DAYS OF CONTINGENCY MANAGEMENT SUPPORTED ABSTINENCE

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Drug Category Cannabis/Cannabinoids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: The goal of this study is to quantify the effect of 30 days of continuous cannabis abstinence on subsequent cannabis use patterns.
Methods: Healthy, non-treatment seeking adolescents who used cannabis at least weekly (n=194) were randomized to either 30 days of cannabis abstinence using contingency management (CM; n=108) or cannabis use monitoring without an abstinence requirement (Mon; n=86). Abstinence was assessed by self-report and verified with a quantitative assay of urine for cannabinoids at each visit. At the end of the 30-day period participants had a follow-up visit at either two weeks (n=85) or 30 days later (n=109).
Results: After the 30-day abstinence period 61.1% of CM participants (n=66) indicated that they wanted to reduce their cannabis use or abstain entirely. At the follow-up visit, CM participants had significantly reduced the average number of days per week that they used cannabis (mean change: MC=1.18, p=0.0002), the average number of times they used cannabis per day (MC=0.62, p=0.0007), and the average number of grams they used per occasion (MC=0.82, p=1.13x10-5) compared to their use at baseline. These differences were significant for the participants who were followed up at two weeks and those who were followed up at 30 days. Participants in the Mon group did not differ in the number of days per week or the number of times per day that they used cannabis at follow-up compared to baseline suggesting that completing a period of abstinence drives the reduction in use in the CM group.
Conclusions: These analyses demonstrate the potential utility of a contingency management supported period of abstinence to precipitate cannabis use changes among adolescents who are not seeking treatment. Future studies are needed to assess the extent to which this reduction in use persists past 30 days.
Financial Support: MC was supported by the Louis V. Gerstner III Research Scholar Award from the Gerstner Family Foundation. JG, AE, and RS were supported through funding from the National Institute on Drug Abuse (R01DA042043, K24DA030443, and K23DA042946, respectively)

CONTINGENCY MANAGEMENT AND SARS-COV-2 TESTING AMONG PEOPLE WHO INJECT DRUGS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: People who inject drugs (PWID) are especially vulnerable to morbidity and mortality as a result of SARS-CoV-2 infection because of social and physical health vulnerabilities. Routine testing for SARS-CoV-2 is critical to reduce transmission. Contingency management (CM)—the provision of tangible rewards to reinforce positive behavior—can promote the use of health services among PWID. Evidence is scarce on the utility of contingency management to promote SARS-CoV-2 testing. The objective of this study was to evaluate the potential for CM to increase testing among PWID.
Methods: SARS-CoV-2 testing was implemented at 9 syringe exchange program sites in partnership with an Oregon-based nonprofit organization for 5 weeks without CM and for 6 weeks with CM (a $10 financial

incentive for testing) from February 1, 2021, through mid-April 2021. We measured rates of testing among syringe exchange program clients before and after implementation of contingency management.
Results: Before contingency management, SARS-CoV-2 testing occurred during approximately 131 of 1410 (9.3%) client encounters and 123 of 997 (12.3%) unique clients were tested. During CM, testing occurred during approximately 571 of 1756 (32.5%) client encounters, and 407 of 1151 (35.4%) unique clients were tested. Rates of testing increased from 0.04 (SD, 0.04) before CM implementation to 0.24 (SD, 0.15) during implementation ($t8 = -4.30$; $P = .003$; Cohen $d = 1.36$).
Conclusions: CM was associated with SARS-CoV-2 testing among PWID. CM may be an effective strategy for improving communicable disease testing beyond testing for SARS-CoV-2 and may also be an effective strategy for improving vaccine uptake among PWID and warrants additional research.
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A CLINICAL COMPARISON OF FIXED AND ESCALATING INCENTIVE SCHEDULES ON COCAINE ABSTINENCE IN CONTINGENCY MANAGEMENT

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Contingency management (CM) interventions are the most effective psychosocial interventions for substance use disorders. However, there are several underdeveloped areas of CM research that require further investigation to create the most robust intervention possible. This study aimed to compare fixed versus escalating and resetting alternative reinforcers on cocaine abstinence in an outpatient trial.
Methods: The procedures and participants discussed in this manuscript are from a larger randomized controlled trial aimed at demonstrating the effects of reduced cocaine use on cardiovascular, immune, and psychosocial function. In this analysis, thirty-four treatment-seeking individuals (18 male, 16 female) with moderate to severe CUD were provided either fixed incentives, in which they received the same value incentive for each benzoylecgonine-negative urine sample they provided, or escalating and resetting incentives, where the value of each incentive increased with every consecutive benzoylecgonine-negative urine sample and reset to the initial level upon a positive sample. Within all conditions, participants received either high value or low value incentives, or were in a non-contingent control group. A generalized estimating equation was used to analyze drug test results: dichotomous outcomes measures (positive/negative) which were repeatedly assessed over 36 timepoints for each participant with results being reported as odds ratios (OR) and 95% confidence intervals (CI).
Results: Escalating and resetting reinforcer values did not have a differential effect on cocaine abstinence or consecutive negative urine samples compared to fixed reinforcer values ($p = 0.603$). Abstinence was best predicted by the magnitude of the incentive, rather than the schedule in which it was delivered ($p = .006$, $OR = 4.210$).
Conclusions: This study contributes to a limited body of literature on the comparative efficacy of fixed and escalating reinforcement schedules on drug abstinence. Future research comparing fixed and escalating schedules on cocaine abstinence in a randomized control trial with a larger sample size is required.
Financial Support: This research was supported by grants from the National Institute on Drug Abuse (R01DA043938; T32DA035200) of the National Institutes of Health.

CLINICAL PHARMACIST-DELIVERED CONTINGENCY MANAGEMENT TO PROMOTE SMOKING CESSATION AMONG PERSONS WITH HIV: INITIAL EXPERIENCES FROM THE SMARTTT TRIAL

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Drug Category Nicotine/Tobacco
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Persons with HIV (PWH) are particularly vulnerable to the health effects of tobacco smoking, yet infrequently receive evidence-based cessation interventions, such as contingency management (CM). We describe initial experiences with clinical pharmacist delivered-CM for smoking cessation among PWH as implemented in the A SMART approach to treating tobacco use disorder in persons with HIV (SMARTTT) trial.
Methods: SMARTTT is a clinical trial with two-stage randomization being conducted in three health systems in the northeastern United States; participants may be offered 5 or 10 CM sessions over 24 weeks depending on randomization and response. Clinical pharmacists underwent didactic and role-play CM training and use structured encounter forms to guide sessions. Sessions are audio-recorded and video group supervision is provided monthly. A CM expert rated sessions for fidelity on CM-specific, general counseling and medication-related items using the CM Competency Scale (CMCS; range 1 [Very Poor] to 7 [Excellent]).
Results: To date, 71 participants have been assigned to receive at least one CM session delivered by one of seven trained clinical pharmacists, and 173 session recordings have been reviewed. CM session attendance ranged from 67.6% attending the week-1 session, to 50.9% attending the week-12 session, to 27.3% attending the week-24 session. CMCS data revealed scores of 5.2/7 (SD = 1.1) for CM-specific items, 5.9/7 (SD = .8) for general counseling items, and 5.4/7 (SD = 1.0) for smoking cessation medication-related items.
Conclusions: Preliminary data show clinical pharmacists can implement CM for smoking cessation among PWH with high fidelity and moderate ongoing supervision.
Financial Support: This work is funded by the National Cancer Institute (R01CA243910).

ORAL COMMUNICATION: MONOCLONAL ANTIBODIES

THE EFFECTS OF A HUMANIZED ANTI-COCAINE MONOCLONAL ANTIBODY ON SINGLE COCAINE DOSE REINSTATEMENT

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The humanized anti-cocaine monoclonal antibody (h2E2) is a lead candidate as a treatment for relapse prevention and increased both the priming and satiety thresholds in the rat self-administration paradigm. Another animal model of relapse is the measurement of lever-pressing behavior after single cocaine injection. The aim was to establish whether h2E2 influences the single-dose cocaine reinstatement model.
Methods: Male adult Sprague-Dawley rats were trained to self-administer cocaine on an FR1 schedule. Rats were switched to a single cocaine dose (12 µmol/kg, i.v.) reinstatement procedure and all lever-pressing behavior was recorded following the infusion. After 6 consecutive daily sessions rats were infused with the vehicle for three daily sessions and then 4.8 µmol/kg of h2E2, all followed by the single cocaine injection. The single cocaine dose sessions were run over the next 22 days.
Results: The latency to lever-pressing following buffer or h2E2 was 15.2 minutes and 5.6 minutes, respectively. This 3-fold reduction in latency was consistent with an increase in the calculated cocaine satiety threshold from 3 µmol/kg to 7.4 µmol/kg in the absence and presence of h2E2, respectively. The duration of lever-pressing behavior also decreased in the presence of h2E2 from a mean of 26.1 minutes to 4.8 minutes. Over the period of 22 days, the effects of h2E2 gradually declined, reaching 50% magnitude of effect after 7-days.
Conclusions: The decreased latency to responding is consistent with a reduced time for the cocaine level to fall to the apparently elevated satiety threshold. The initial 5-fold decrease in the duration of lever-pressing

behavior is consistent with increases in both the satiety and priming thresholds in the presence of h2E2. The effect of h2E2 on latency and duration of activity declined over 22-days consistent with the half-life of h2E2. The duration of any relapse event in the presence of h2E2 may be greatly reduced.
Financial Support: U01DA050330

CHARACTERIZATION OF OPIOID-SPECIFIC MONOCLONAL ANTIBODIES ISOLATED FROM OPIOID USE DISORDER PATIENTS AND THE RELEVANCE OF OPIOID-SPECIFIC FAB STRUCTURES TO EFFICACY AND SELECTIVITY

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: To validate and compare the binding affinities of mAbs isolated from naive individuals and unvaccinated OUD patients; to probe beneficial residues that facilitate opioid-mAb interactions on lead humanized mAbs candidates against fentanyl and carfentanil.
Methods: The blood samples were processed to PBMC.Oxycodone and morphine-specific B cells were pulled down using antigen-specific, magnetic-based dual enrichment with OXY-SA-PE and MOR-SA-PE. A global transcriptomic map was generated to distinguish the antigen-specific B cell population, and B cell receptor (BCR) sequencing was performed to generate the sequence of Fv region of the corresponding mAb. The identified Fv regions were grafted onto human IgG1 scaffold and expressed in cell line Expi293. The binding affinities were tested using in vitro Octet kinetic test. The cross-reactivities against target (oxycodone) and off-target (morphine, heroin and naloxone) drugs were validated using competitive ELISA. The structure of drug-Fab complex was solved using X-ray crystallography and the beneficial residues were identified. The strength of the interaction was validated using site-direct mutegenesis and the residues were replaced with alanine. The binding affinities were also checked by Octet.
Results: Opioid use yields to a higher frequency of oxycodone-specific B cell populations; there are more morphine-specific B cells than oxycodone-specific B cells in humans regardless of the drug-naïve or OUD status; mAbs isolated from unvaccinated OUD patients showed affinity against morphine. The human mAbs also showed cross reactivity to heroin and no cross reactivity to naloxone.
When substituted with alanine on the positions of beneficial residues, the humanized mAbs demonstrated increased Kd, or even no detectable binding.
Conclusions: OUD can increase the presence of opioid-specific B cell populations and functional antibodies.
The beneficial residues facilitated the drug-mAb binding while the disruption of the residues can affect the efficacy of the mAbs.
Financial Support: U01 DA051658;UG3 DA047711

MONOCLONAL ANTIBODIES DISPLAYING MUTATIONS IN FC REGION TO PROLONG PROTECTION AGAINST FENTANYL TOXICITY

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Drug Category Opiates/Opioids
Topic Molecular Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: To increase the duration of efficacy of a lead chimeric fentanyl-specific mAb
Methods: 36 Mice all male
We introduced three different mutations to the Fc region of the mAb using site-directed mutagenesis. Biolayer interferometry was used to test binding affinity of mutated mAb to FcRn. Efficacy of the mutated

and WT mAb against fentanyl-induced behavior and toxicity was also tested in mice. Finally, the half-life and long-term efficacy of these mutated mAbs was assessed in transgenic mice expressing human FcRn.
Results: Biolayer interferometry paired with recombinant FcRn showed a 10-fold increase in affinity of the recombinant mAb compared to wild-type. Efficacy of the mutated and WT mAb against fentanyl-induced behavior and toxicity was also tested in mice. Both the mutated and WT mAb reduced fentanyl-induced antinociception, respiratory depression, and bradycardia. Finally, the half-life and long-term efficacy of these mutated mAbs was assessed in transgenic mice expressing human FcRn. Extending the half-life of these mAbs will facilitate more successful clinical approaches in preventing opioid-related overdoses.
Conclusions: Extending the half-life of these mAbs will facilitate more successful clinical approaches in preventing opioid-related overdoses.
Financial Support: NIDA under CounterACT grant U01-DA051658

BISPECIFIC MONOCLONAL ANTIBODIES PROTECT AGAINST TOXICITY FROM FENTANYL AND CARFENTANIL

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Biologics including vaccines and monoclonal antibodies (mAb) have been explored as alternative or complementary treatments for substance use disorder, and vaccines against opioids including fentanyl have shown significant preclinical efficacy. In contrast to current opioid receptor antagonist medications targeting brain receptors, antibody-based therapeutics bind fentanyl in circulation and prevent its interaction with receptors in the brain. However, because of the high specificity of mAb for target drug, a limitation of fentanyl-specific biologics is the increasing risk of fentanyl analogs, such as carfentanil, appearing in street mixtures of opioids and stimulants. Hence, development of vaccines and mAb that are able to target multiple fentanyl analogs is critical.
Methods: A heterologous prime-boost strategy was used to isolate murine hybridomas expressing mAb that bind both fentanyl and carfentanil. Mice (n=4 per group) were primed with either a fentanyl- or carfentanil-specific conjugate vaccine, followed by a cross-specific boost at a later time. Hybridomas were generated from splenocytes of vaccinated mice, and screened for expression of mAb specific for fentanyl, carfentanil, or both. Isolated mAb that showed high affinity for both fentanyl and carfentanil by biolayer interferometry were sequenced and cloned into vectors expressing human antibody Fc to generate chimeric mAb.
Results: Chimeric anti-fentanyl/carfentanil mAb retained binding to both drugs compared to hybridoma-expressed murine mAb, measured by competitive ELISA. To evaluate efficacy of bispecific mAb in vivo, mice were passively immunized with 40 mg/kg bispecific mAb, and challenged with either fentanyl, carfentanil, or a combination. Passively immunized mice showed reduced effects from drugs, including on opioid-induced antinociception, bradycardia, and respiratory depression.
Conclusions: These results indicate that the heterologous prime-boost method utilizing multiple structurally distinct vaccines can be used to isolate mAb with broader specificity for opioids, and support further pre-clinical development of mAb targeting multiple fentanyl-class compounds.
Financial Support: This work is supported by NIDA CounterACT program under grant U01-DA051658.

ORAL COMMUNICATION: ROLE OF SEX/GENDER ON SUDS

ESTRADIOL ENHANCES THE EXPRESSION OF ADDICTION-LIKE FEATURES IN A FEMALE RAT MODEL OF OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Animal Study
Abstract Category Original Research

Aim: Despite higher rates of substance use disorder in men than women, women are more vulnerable than men on many aspects of disease. Female animals also display an enhanced vulnerability to developing addiction-like features with evidence indicating that estradiol underlies this enhanced vulnerability. However, most of this evidence is for psychostimulants and alcohol; evidence with opioids is sparse, and to our knowledge, no studies have examined the impact of estradiol in rat models of opioid use disorder.
Methods: The development of two key addiction-like features, an enhanced motivation for fentanyl, as assessed using a progressive-ratio schedule, and vulnerability to relapse, as assessed using an extinction/cue-induced reinstatement procedure, were determined in separate groups of ovariectomized (OVX) female rats with (n=10) and without estradiol (n=8-10) replacement. Effects were determined following extended, 24-hr/day access to fentanyl (fixed-ratio 1 access during 5-min trials that initiated every 30 min for 10 days) and 14 days of withdrawal.
Results: Rats with estradiol self-administered more fentanyl and showed an enhanced sensitivity to the reinstating effects of fentanyl-associated cues compared to rats without estradiol. Rats with estradiol also showed an increase in motivation for fentanyl following withdrawal from extended-access fentanyl self-administration (relative to the pre-extended-access baseline), whereas motivation was not changed from baseline in rats without estradiol.
Conclusions: These results indicate that, as with findings with psychostimulants and alcohol, estradiol enhances the development of an opioid addiction-like phenotype in females.
Financial Support: This work was supported by NIDA grants R01DA024716 and R21DA049992 (WJL) and a Pharmacological Sciences Training Grant 5T32GM007055-47 and a Wagner Fellowship from the University of Virginia (EBT)

EFFECTS OF ESTRADIOL AND PROGESTERONE FLUCTUATIONS ACROSS THE MENSTRUAL CYCLE ON CEREBRAL BLOOD FLOW: A LONGITUDINAL PERFUSION FMRI STUDY IN NATURALLY CYCLING WOMEN

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Compared to men, women suffer greater health consequences from smoking cigarettes and generally are less successful at quitting smoking. Hormones, specifically estradiol (E) and progesterone (P) that fluctuate over the course of the natural menstrual cycle (MC), may contribute to these sex differences. The time of the MC when E is high and unopposed by potential protective effects of P, the late follicular phase, is associated with a greater experience of reward. We hypothesized that reward-related brain circuits would demand greater cerebral blood flow (CBF) to nourish and replenish active regions during this state of high arousal. This longitudinal study aimed to quantify CBF within a priori regions of interest (ROIs) over the course of three MCs in naturally cycling women who are chronic cigarette smokers.
Methods: Fifteen women completed biochemical, hormonal verification visits and three laboratory/neuroimaging test days (TDs). TDs included acquiring saliva-based hormone levels and a resting state perfusion fMRI scan that provides a quantitative measure of CBF. Women smoked to satiety ~90m prior to data acquisition. TDs were randomized by MC phase and timed to occur when hormonal differences were greatest; early follicular phase (low E, low P; LEP), late follicular phase (high E, unopposed by P; HE) and mid-luteal phase (high E, high P; HEP). Data were analyzed using statistical parametric mapping ver12. ROIs included the ventral and dorsal striatum, medial orbitofrontal cortex, dorsolateral prefrontal cortex (dlPFC), anterior ventral insula and subgenual anterior cingulate.
Results: CBF was greater during HEP and HE compared to LEP ($p=0.038$ familywise-error corrected) in the dlPFC (x,y,z: 18,60,18). CBF was not affected by hormone fluctuations in other ROIs or contrasts.
Conclusions: Unprovoked by task or drug, CBF is reduced in the dlPFC, a region that plays a pivotal role in decision-making, during LEP, when hormone influences are lowest.
Financial Support: R01DA040670

GENDER DIFFERENCES IN ANTECEDENTS OF CANNABIS USE

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Drug Category Cannabis/Cannabinoids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Identifying motives for cannabis use is critical to the development of effective interventions, and motives may differ by gender. The Inventory of Drug Taking Situations (IDTS) assesses the types of situations in which individuals most often use drugs through eight subscales: dealing with (1) Unpleasant Emotions; (2) Physical Discomfort; (3) Pleasant Emotions; (4) Testing Personal Control; (5) Urges/Temptations; (6) Conflict with Others; (7) Social Pressure; and (8) Pleasant Times with Others. The aims of this study were to determine if IDTS scores varied by gender in individuals with CUD, and if cannabis use or CUD severity were associated with specific use situations.
Methods: Baseline data were obtained from an ongoing study of 130 non-treatment-seeking individuals with CUD. Gender differences in demographic characteristics were compared using Wilcoxon-Rank sum and Chi-square tests. Generalized linear models were used to assess associations between IDTS subscale scores and recent cannabis use/CUD severity. Associations of CUD severity with high/low endorsement of using situations (median split) were assessed using ordinal and binary logistic regression modeling.
Results: Women reported using cannabis more than men in response to conflict with others, testing personal control, physical discomfort, and unpleasant emotions (all p's<0.05). Subscale scores for unpleasant emotions, pleasant emotions, and conflict with others were positively associated with recent cannabis use across genders. When examining the high/low endorsement of use for pleasant emotions, unpleasant emotions, neither, or both, women, but not men, were more likely to endorse use for unpleasant emotions; the same pattern was observed when limiting analysis to individuals with severe CUD.
Conclusions: Findings suggest significant gender differences in motivations for cannabis use and coping with unpleasant emotions may be more prevalent in women. Appreciation of motives unique to women that use cannabis can aid in the development of tailored strategies to help patients cope with high-risk situations as part of treatment.
Financial Support: NIDA T32-DA007288, U54-DA016511

GENDER AND CHRONIC PAIN AS RISK FACTORS FOR GREATER OPIOID WITHDRAWAL SEVERITY

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: There is substantial variability in the severity of opioid withdrawal across patients that differ according to demographic and clinical characteristics. It is not well understood whether differences exist at treatment presentation or emerge in response to treatment. This study examined the relative contribution of demographic and clinical characteristics on withdrawal severity from intake to 7-9 days after treatment intake.
Methods: The sample included 1,252 individuals ≥ 18 years old entering residential substance use disorder (SUD) treatment in the United States. These individuals completed demographic, clinical, and substance use questions at intake. They were assessed for this study's primary outcome, opioid withdrawal severity, at intake and at 1-3, 4-6, and 7-9 days after intake. A fixed effects mixed model was used to determine the impact of gender and chronic pain status on self-reported opioid withdrawal severity at the time of treatment presentation and over the course of treatment. Covariates in the model included age, opioid of choice, SUD severity, and presence polysubstance use.
Results: The results indicated that women and people with chronic pain present for treatment with the highest withdrawal severity. Withdrawal decreased over time in the same linear manner, independent of gender and chronic pain, suggesting that the differences observed were related to greater severity at time of

intake rather than differential response to treatment. Being older, having greater substance use severity, and engaging in polysubstance use were associated with elevated opioid withdrawal symptoms at intake.
Conclusions: This study expands our understanding of opioid withdrawal severity by identifying women and people with chronic pain as groups who may express more severe opioid withdrawal during residential SUD treatment. These findings suggest that more intensive withdrawal treatments may need to be considered for these groups and reveal potential biological mechanisms (e.g. chronic pain) that affect opioid withdrawal severity.
Financial Support: T32DA007209 (Bigelow/Strain/Weerts)

ORAL COMMUNICATION: PRENATAL SCIENCE 1

MITRAGYNINE AND NEONATAL OPIOID WITHDRAWAL SYNDROME (NOWS) IN RATS

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Drug Category Opiates/Opioids
Topic Prenatal/Perinatal
Abstract Detail Animal Study
Abstract Category Original Research
Aim: There are reports of women using kratom (Mitragyna speciosa) during pregnancy resulting in newborns displaying symptoms of neonatal opioid withdrawal syndrome (NOWS). The most abundant psychoactive component of kratom leaves is mitragynine. This preliminary study evaluated rat neonates after prenatal exposure to mitragynine to determine if symptoms of NOWS are present.
Methods: Sprague Dawley rats (N=4, each group) were orally dosed twice a day with either vehicle (0.5 mL), morphine (escalating dose; 5 mg/kg to 32 mg/kg), or mitragynine (20 mg/kg) from conception through birth. Within 24 hours of birth, behavioral testing was conducted. Naltrexone (1 mg/kg, i.p.) or saline (0.5 mL/kg, i.p.) (N=17, each treatment) was administered to precipitate withdrawal or to act as a control, respectively. After 5 minutes, neonate behavior was recorded for 10 minutes using ANY-maze software to calculate distance travelled and mean speed. Additional behavior including headshaking, body stretches, paw treading, and rolling were hand-scored using a binning method that recorded whether the pup exhibited that behavior every 30 seconds of the test (i.e., highest score=20). Neonate behavior from each treatment combination was compared using two-way ANOVA test with post-hoc Bonferroni's multiple comparisons.
Results: There were no significant differences between neonates exposed to morphine or mitragynine for all categories, except rolling (adjusted P=0.0006). There were statistically significant differences between morphine and vehicle and between mitragynine and vehicle, (adjusted P-values between 0.0424 and <0.0001) except rolling.
Conclusions: The results of this preliminary study indicate that prenatal exposure to mitragynine may result in symptoms of NOWS. The results are concerning and further work looking into the effect of mitragynine on fetal and neonatal development must be performed. Kratom is a complex natural product that contains many compounds (≥40 alkaloids) that must also be considered when examining the effects seen in humans.
Financial Support: None

FACILITATING TREATMENT ENTRY AND CONTRACEPTION IN POSTPARTUM NICU MOTHERS WHO USE SUBSTANCES

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Drug Category Other, Cannabis, stimulants, hallucinogens, benzos, polydrug
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: The primary aim of the study was to test a brief motivational interviewing plus acceptance and commitment therapy intervention to facilitate treatment initiation and reproductive planning postpartum among NICU mothers who used substances during pregnancy.

Methods: Mothers (N = 64) with an infant admitted to a neonatal intensive care unit were enrolled if they or their infant tested positive for an illicit substance at delivery or had a documented positive drug screen during pregnancy. A parallel group, randomized controlled design assigned participants to MIACT or conventional care (CC), with assessments at week 2 and 4 during treatment and follow-up at 2 and 6 months post treatment. Groups were stratified on type of drug used (marijuana only vs. other or poly-drug use). Bayesian generalized linear modeling was used to evaluate outcomes as a function of treatment using an intent-to-treat approach.
Results: Results indicated that during treatment the MIACT group demonstrated an 84% probability of benefit relative to CC with regard to facilitating treatment initiation, with a 56% and 74% probability of benefit at the 2 and 6 month follow-up, respectively, with the highest relative risk of 1.5 during treatment. MIACT was also associated with an increased probability of attending a postpartum obstetrics visit (RR = 1.4), and receiving contraception during treatment and at follow-up, with posterior probabilities close to 99% and relative risks ranging from 1.5 – 5.1. Mothers using marijuana only were less likely to engage in treatment, attend an obstetrics visit, or receive contraception relative to women using other drugs or multiple drugs.
Conclusions: Brief, hospital-initiated interventions can assist postpartum mothers who use substances to enter treatment and to obtain contraception in order to reduce future substance-exposed pregnancies. Future iterations of the intervention need to better address those who smoke marijuana only.
Financial Support: NIH/NIDA R34DA041465

THE PREVALENCE OF PRENATAL FENTANYL EXPOSURE AND CO-EXPOSURE TO COMMONLY ABUSED DRUGS IN A HIGH-RISK POPULATION

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Drug Category Opiates/Opioids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Prenatal exposure to fentanyl may lead to Neonatal Abstinence Syndrome (NAS), a constellation of symptoms observed when newborns begin withdrawing from addictive substances such as opioids. The use of umbilical cord (UC) for newborn toxicology has been increasing due to its apparent long detection window, sensitivity, and ease of collection. However, very little has been reported in the literature concerning the prevalence of in utero exposure to fentanyl and co-exposure with other commonly abused substances. The specific aims of this study are twofold. We will report prevalence of neonatal exposure to fentanyl for a nationwide high-risk population using UC submitted to a national reference laboratory and the co-exposure patterns observed for these fentanyl-exposed neonates.
Methods: A secondary analysis was performed using historical data for UC received between 1/01/2020 and 12/31/2020 for routine toxicology analysis.
Results: Our laboratory received 23,104 UC and 9667 (41.8%) of those UC were positive for at least one drug. The prevalence of fentanyl was 1.9% (n = 429). There were 407 UC where both fentanyl and norfentanyl were detected. When detected, the median concentrations of fentanyl and norfentanyl were 3916 pg/g (IQR: 1696, 9230 pg/g) and 10717 pg/mg (IQR: 3925, 25288 pg/g), respectively. Of the 429 positive fentanyl and/or norfentanyl UC, 33 (7.7%) were only positive for fentanyl and/or norfentanyl. Of the 396 polypositive UC, morphine was the highest co-exposure with 243 UC (56.6%). The second most prevalent co-exposure observed was methamphetamine/amphetamine (n = 173; 40.3%) followed by cannabinoids (n = 113; 26.3%) and benzoylecgonine (cocaine metabolite; n = 106; 24.7%).
Conclusions: Nonmedical use of fentanyl is an alarming trend in this country including the maternal demographic reported here. In the majority of cases included in this study, we found that prenatal exposure to fentanyl also included exposure to other commonly abused substances.

CO-USE OF OPIOIDS WITH METHAMPHETAMINE AMONG PREGNANT WOMEN IN SUBSTANCE USE DISORDER TREATMENT, 2006-2018

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: A twin-epidemic of opioid and methamphetamine overdoses has emerged, with methamphetamine-involved overdoses rising fivefold between 2012 and 2018. Co-use of heroin and methamphetamine doubled between 2015 and 2019 in the general population and increased among people seeking substance use disorder treatment from 1 in 50 in 2008 to 1 in 8 in 2017. The goal of the present study was to examine temporal trends in co-use of opioids and methamphetamine among pregnant people seeking substance use disorder treatment and associated sociodemographic and treatment variables.
Methods: Data were concatenated from the 2006-2018 Treatment Episodes Database – Discharges public use files. Only variables collected in all years were included and analyses were restricted to cases where the individual was pregnant at their admission to treatment and reported opioid use as the primary drug leading to the treatment episode (N=94182). Cochrane-Armitage trend tests analyzed changes over time and chi-square and regression analyses analyzed associations between co-use and treatment and demographic variables.
Results: Co-use of opioids and methamphetamine among pregnant women in substance use disorder treatment significantly increased from 5.6% of cases in 2006 to 22.0% in 2018. Women who co-used were significantly less likely to receive medications for opioid use disorder compared to women who did not co-use, 33.7% vs. 46.6%, respectively. Use of medications for opioid use disorder for women who co-used was unchanged despite an increase from 47.1% to 58.4% among women who did not co-use. Co-use was not strongly associated with length of treatment or treatment outcomes.
Conclusions: Co-use of opioids and methamphetamine among pregnant women in substance use disorder treatment rose fourfold from 2006 to 2018. The vast majority of pregnant women who co-use are not receiving medications for opioid use disorder despite being the universally recommended standard of care. Further research and efforts are needed to eliminate this inequity.
Financial Support: Pennsylvania Department of Drug and Alcohol Programs #4100088715 R1

ORAL COMMUNICATION: SEXUAL MINORITY HEALTH AND SUDS

EXPLORING CORRELATES AND TYPES OF SEXUAL MINORITY STRESS: A LATENT PROFILE ANALYSIS

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Drug Category Stimulants
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Sexual minority men (SMM) experience stress as a result of stigma and discrimination which may partly explain elevated rates of substance use and mental health disorders. Few studies have explored different facets of sexual minority stress in men living with HIV who use substances. This study sought to identify the profiles of sexual minority stress specific to SMM living with HIV who use methamphetamine and examine correlates of profile membership (e.g., substance use severity).
Methods: This cross-sectional study enrolled 110 SMM living with HIV who had biologically confirmed, recent methamphetamine use in San Francisco. We utilized a latent profile analysis to characterize underlying patterns of covariance of sexual minority stress to identify 'profiles' or sub-groups of participants. Participants completed self-report measures of sexual minority stress including: internalized homophobia, concealment of sexuality, expectations of rejection, and prejudice events (i.e., discrimination, violence). ANOVA and Chi Square analysis were used to examine the correlates of profile membership including measures of drug use (e.g., Addiction Severity Index) and mental health.
Results: Participants were on average 43 years old (SD = 9), Non-White (57%), and had been diagnosed with HIV for an average of 13 years (SD = 9). Four distinct profiles of sexual minority stress emerged: (a)High Concealment (b)Low Concealment, High Prejudice Events (c)Low Sexual Minority Stress and (d)High Sexual Minority Stress. The High Minority Stress profile had significantly higher addiction severity than those with low minority stress (p=0.001). Each profile had clinically meaningful mean levels of PTSD

and depression. Men with greater depressive symptoms (p=0.003) and severe PTSD (p=0.001) had higher probabilities of membership in profiles with high sexual minority stress.
Conclusions: Findings underscore that addressing minority stress could optimize substance use treatment outcomes and mitigate co-occurring depression and PTSD, but additional research is needed to elucidate other facets of stress in SMM who use substances.

THE MODERATING EFFECT OF STATE LGBT YOUTH POLICIES ON PRESCRIPTION DRUG MISUSE IN GENDER MINORITY COLLEGE STUDENTS

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Drug Category Other, Prescription opioids, stimulants, and tranquilizer/sedatives
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Evidence suggests that discriminatory state-level policies towards gender minority (i.e., transgender and non-binary) individuals are linked to poorer health and greater experiences of bullying in adolescents. Our aim was to examine whether state policies towards LGBT youth moderate prevalence of prescription drug misuse (PDM) in matriculating US undergraduate and graduate college/university students.
Methods: Data were from the 2016-17 AlcoholEdu prevention program baseline data (N = 419,185, 97.3% undergraduate, 56.4% female sex at birth, 61.6% white); 3,340 who were gender minorities (0.8%). Data included 14-day PDM involving stimulant, opioid, or tranquilizer/sedative medication and the state from which the respondent graduated high school (HS). HS state was linked to the 2017 Movement Advancement Project data quantifying aggregate state-level policies affecting LGBT youth (e.g., bans on transgender youth sports participation). Prevalence of any 14-day PDM and PDM by medication class were calculated by gender identity and then among gender minority students by policy level.
Results: Or any PDM (8.2% for gender minority, 2.4% for cis-gender) and PDM by medication class, gender minority students had higher rates of misuse than cis-gender students (ps < 0.001). Within gender minority students, any 14-day PDM and stimulant PDM were significantly elevated in matriculating students from states with a negative policy environment (11.3% and 8.0%, respectively) versus those from low, medium, or high equality states (7.0% and 3.6%, respectively. Opioid or tranquilizer/sedative PDM did not differ by state-level LGBT youth policies.
Conclusions: Gender minority matriculating college students have elevated rates of any PDM and PDM by medication class, versus cis-gender students, and negative state-level policies may influence rates of any PDM and stimulant PDM in gender minority students. This suggests that gender minority individuals may warrant specific screening for PDM and that advocacy for policies fostering equality may limit PDM in this vulnerable group.

SUBSTANCE USE AND CO-MORBID HEALTH OUTCOMES OF BLACK WOMEN AND LGBTQ+ INDIVIDUALS WITH OUD ENROLLED IN AN OUTPATIENT TREATMENT PROGRAM

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Black women and LGBTQ+ individuals who have Opioid/Other Drug Use Disorders often have comorbidities including PTSD and HIV/HCV and face significant barriers to care. To provide easily accessible and comprehensive care to these populations, the BRITER Program (Bringing Resources Individually to Engage Recovery) was initiated within an outpatient MOUD treatment clinic. The present study examined substance use and co-morbid health outcomes at 6 months post-enrollment in BRITER.
Methods: This study included 136 participants that were recruited from the existing clinic population from 2019-2021, with an emphasis on those in treatment for less than 30 days. All participants received MOUD,

counseling, case management and were offered HIV/HCV testing and HCV treatment. All completed standardized measures at baseline, including the GPRA, LEC-5, PCL-5 and HIV/AIDS Risk Assessment. 92 participants (75 Black women and 17 LGBTQ+ individuals) completed these measures at 6 months post-enrollment. Only these participants were included in analysis of substance use and mental health outcomes. Paired samples t-test and McNemar's chi-square test were used to evaluate significance.
Results: Number of participants reporting recent (past month) drug use decreased from 56% at baseline to 41% at 6 months ($p = .007$). Days using drugs also decreased from 8.94 to 4.88 days ($p < .001$). There were no changes in days feeling depressed or anxious in the past month, but there was a trend toward a decrease in PTSD symptom severity score (on a scale of 0-80) from 57.03 to 33.07 ($p = .066$). Psychological distress (on a scale of 0-4) increased from 1.84 to 2.20 ($p = .049$). 22 participants (16%) tested positive for HCV. Of those, 12 (55%) were successfully treated through BRITER.
Conclusions: Our results suggest modest, but limited reduction in substance use, mental health symptoms and HCV infection as a result of participation in BRITER.
Financial Support: This research was supported by SAMHSA Grant TI080619.

SOCIAL ECOLOGICAL INFLUENCES ON NICOTINE/TOBACCO USE AMONG GENDER-FLUID AND GENDER-STABLE ADOLESCENTS AND ADULTS IN THE U.S.

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Drug Category Nicotine/Tobacco
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Transgender individuals have increased risk of nicotine/tobacco use relative to cisgender populations. Yet, there remains limited knowledge of nicotine/tobacco use among gender-fluid individuals (i.e., people whose gender identity changes over time). Guided by the social ecological framework, we examined individual-, interpersonal-, community-, and policy-level factors affecting nicotine/tobacco use among U.S. adolescents and adults who are fluid or stable in their gender identities.
Methods: We conducted secondary analyses of Waves 2-4 (2014/15-2016/18) of the nationally representative Population Assessment of Tobacco and Health Study (n=33,197 U.S. individuals aged ≥14 years). We used multivariable logit models to assess the associations of gender stability/fluidity over three waves with past 30-day nicotine/tobacco use (i.e., any, cigarette, e-cigarette, other tobacco, and poly-tobacco) at Wave 4 as a function of psychological distress, number of tobacco products used by close family/friends, channels of exposure to nicotine/tobacco marketing and change in state-level policy environment relevant to gender minorities from 2015 to 2017 (from the Movement Advancement Project), adjusting for potential confounders.
Results: Gender-fluid individuals had significantly increased odds of all nicotine/tobacco use outcomes (adjusted odds ratios [AOR] 1.8-2.3, $p<.01$), compared with cisgender-stable individuals. High psychological distress and tobacco use among family/friends were positively associated with all nicotine/tobacco use outcomes (AOR 1.7-2.5, $p<.001$, and 1.2-1.3, $p<.001$, respectively). Channels of exposure to nicotine/tobacco marketing and living in a state that improved its policy protections for gender minorities from medium to high decreased the odds of nicotine/tobacco use (AOR 0.9-1.0, $p<.001$, and AOR=0.8, $p<.05$, respectively).
Conclusions: Gender-fluid individuals are at higher risk for nicotine/tobacco use relative to cisgender-stable individuals, placing them at greater risk for nicotine/tobacco-related health consequences. In some cases, improvements in gender minority-related policies were protective against nicotine/tobacco use for all individuals. Our findings underscore the need for awareness of gender diversity and to consider multi-level nicotine/tobacco prevention and intervention strategies.
Financial Support: This research was supported by the National Cancer Institute (R01CA212517 and R01CA203809) and the US Food and Drug Administration (FDA) Center for Tobacco Products (U54CA229974), National Institute on Drug Abuse (R01DA44157, R01DA043696, and R21DA051388).

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ORAL COMMUNICATION: ALCOHOL AND PSYCHIATRIC COMORBIDITIES

ANTERIOR INSULAR CORTEX FIRING ACTIVITY LINKS INITIAL AND SUSTAINED ENCODING DURING AVERSION-RESISTANT ALCOHOL CONSUMPTION

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Drug Category Alcohol
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Compulsive-like alcohol drinking (CLAD), where alcohol intake persists despite adverse consequences, is a core facet of alcohol use disorder and a major clinical obstacle to successful treatment. Recent work has shed light on underlying circuit/neurochemical mechanisms, but much remains unknown. Previously, we described that anterior insula (AINS), a central mediator of emotion and motivation, is critical for promoting CLAD in rodents, and heavy human drinkers show similar insula-circuit recruitment when responding for alcohol under threat of shock. However, global AINS inhibition reduces CLAD and AlcOnly, suggesting that parallel AINS pathways may mediate aversion-resistant versus regular alcohol. One major obstacle to understanding AINS importance for alcohol drinking is the lack of information on in vivo AINS firing patterns during intake, which could shed critical light on the nature of AINS activity that promotes intake.
Methods: We used 32-electrode multi-wire electrophysiology implants to record single-unit activity in right AINS from 15 rats, with two sessions per rat of each of the three drinking condition (AlcOnly; CLAD with 10mg/L or 60mg/L quinine in alcohol). Data is from ~400 neurons per drinking condition.
Results: Studies implicate AINS in both initiation and sustaining of motivated responding, and we find a confluence of these patterns. AINS neurons with a large firing increase at initiation of intake (Initial Response cells) showed significantly larger activity across the rest of licking during CLAD relative to AlcOnly. In contrast, neurons selected by phenotype of sustained firing increases or decreases showed no differences across conditions. There were also significant difference in the first seconds of bottle access under the higher challenge.
Conclusions: AINS cells can show sustained firing across drinking, but only neurons with strong firing at licking onset show greater sustained responding under compulsion-like conditions. We provide critical new information about how AINS, crucial for sustaining alcohol drinking, expresses the drive for alcohol.
Financial Support: R01AA024109

PRO- AND ANTI-INFLAMMATORY BIOMARKERS AS PREDICTORS OF RESPONSE TO VALPROATE IN PATIENTS WITH COMORBID ALCOHOL USE AND BIPOLAR DISORDER- PRELIMINARY FINDINGS

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Drug Category Alcohol
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Bipolar disorder (BD) has the highest association with alcohol (AUD) and other substance use disorders and represent significant treatment challenges. We have previously shown that the GABAergic agonist valproate (VPA) decreases heavy drinking among these patients, however predictors of response to VPA are not known. AUD promotes a pro-inflammatory state while VPA increases levels of anti-

inflammatory factors. We hypothesized that VPA has an anti-inflammatory effect and that patients with AUD/BD who respond to VPA have higher baseline inflammatory indices.
Methods: Nine patients with DSM-IV-defined diagnoses of AUD and BD were enrolled in the study. Patients received a course of VPA for 3 months (average dose 1000 mg/day) in addition to receiving either naltrexone of 50 mg daily or placebo. Liver function tests and trough VPA serum concentrations were evaluated at baseline and periodically. Alcohol use outcome was assessed using the Timeline Follow-Back for Recent Drinking. The primary alcohol use outcome was changes in proportion of weekly heavy drinking days (5 or more drinks/day for men, 4 or more drinks/day for women). Plasma levels of cytokines were measured using Multiplex Immunoassay.
Results: About one half of enrolled patients responded to VPA. Screening of pro- and anti-inflammatory cytokines showed that responders had higher levels of the chemokine SDF-1alpha/CXCL12alpha and the pro-inflammatory marker C-reactive protein (CRP) and lower levels of anti-inflammatory factor matrix metalloproteinase-10 (MMP-10) ($p < 0.05$). Screening of cytokines in samples before and after treatment with VPA showed that VPA increased levels of anti-inflammatory factors interleukin-10 (IL-10) and MMP-10 ($p < 0.05$) and tended to decrease levels of pro-inflammatory CRP ($p > 0.05$).
Conclusions: These preliminary findings suggest that pro- and anti-inflammatory biomarkers may serve as predictors of treatment response to VPA and its therapeutic effect may be in part due to its anti-inflammatory action. Larger studies may be indicated to validate these findings.
Financial Support: Supported by USPHS Grants AA015385

PAST ANXIETY/DEPRESSION SYNDROME T-SCORES AND SUBSTANCE USE DURING COVID-19 IN EARLY ADOLESCENTS FROM THE ABCD STUDY

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Drug Category Other, Alcohol, Nicotine, and Cannabis
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: We examined the association of pre-COVID-19 identified anxiety/depression syndrome t-scores with substance use (alcohol, nicotine, and cannabis) during the COVID-19 pandemic among adolescents. We hypothesized that those with previous anxiety/depression symptoms would have higher odds of substance use during the pandemic, compared to those without anxiety/depression symptoms.
Methods: A total of 3,671 participants enrolled in the Adolescent Brain Cognitive Development (ABCD) Study were included in this study. Past anxiety/depression syndrome t-scores were calculated with the Child Behavior Checklist Scale. Substance use was obtained from the Youth ABCD COVID-19 questionnaire. Age, sex, parents' alcohol/drug use, family income, and simultaneous substance use, were included as potential confounders. Sex was explored as effect modifier. Crude and adjusted mixed effect logistic regression models were fit to estimate odds ratios with study site as a random effect.
Results: The crude odds ratio for higher anxiety/depression syndrome t-scores among the male participants who used nicotine was 0.99 (p-value= 0.04) compared to those with no nicotine use. No statistically significant associations were found for alcohol or cannabis use models among males, or in any model, overall or among females. After adjusting for potential confounders, a significant association between higher anxiety/depression syndrome t-scores and alcohol use was found in the overall sample (AOR=1.06, p-value=0.04) compared to no alcohol use, but not for the analyses stratified by sex. No statistically significant associations were found for nicotine or cannabis use.
Conclusions: Higher pre-pandemic anxiety/depression syndrome t-scores were associated with alcohol use during COVID-19, but not with nicotine or cannabis use. Sex was not found to be an effect modifier in the associations. Future studies are required to understand the effects of previous psychological syndromes during late childhood with substance use during the COVID-19 pandemic.
Financial Support: This study is supported by the NIDA/NIAAA training grant: R25DA051249.

ANALYZING RELATIONSHIPS BETWEEN CHILD NEGLECT AND RISK FOR ALCOHOL USE DISORDER AMONG AT-RISK ADOLESCENTS

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Drug Category Alcohol
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Alcohol use disorder (AUD) is a major concern for adolescent health. Justice-involved adolescents are more likely to have experienced psychological and physical neglect and are more prone to AUD. The is a deficit of knowledge on how diverse measures of psychological and physical neglect may impact risk for AUD among this population. The current study investigates the individual and combined effects of psychological and physical neglect on the odds of AUD.
Methods: Logistic regression was employed to analyze a state-wide sample of 79,960 JIA from the Florida Department of Juvenile Justice (FLDJJ). This sample includes all youth who (a) received one or more arrests for delinquency, (b) completed the full intake assessment, and (c) reached the age of 18 by the year 2016. Past 30-day AUD use was obtained from self-reported data. Interview data was used to create a child neglect index.
Results: More than one in ten adolescents met the criteria for alcohol use disorder, and one in five experienced both psychological and physical neglect. Psychological neglect was associated with 18% higher odds of AUD, and physical neglect was associated with a 58% increased odds of AUD.
Conclusions: The results of this study indicate that intervention efforts that address sources of psychological and physical neglect may help to reduce the risk for AUD before and after adolescents leave the system. Social programs that help caregivers provide for their children's psychological and physical needs may play a vital role in preventing alcohol-related problems.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the authors' responsibility and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

ORAL COMMUNICATION: HOW DO FLAVORINGS INFLUENCE NICOTINE USE BEHAVIORS

COMPARISON OF CIGARETTE DEPENDENCE BETWEEN ADULT MENTHOL AND NON-MENTHOL SMOKERS

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: While all cigarettes are addictive, some researchers have found that menthol cigarettes are likely associated with increased dependence. We present the secondary data analysis to investigate the association between menthol smoking and dependence based on the recent Population Assessment of Tobacco and Health (PATH) Study data.
Methods: We conducted cross-sectional analysis of the PATH Wave 4 data to compare cigarette dependence among adult (18 years or older) current menthol (n=3,904) and nonmenthol (n=5,331) cigarette smokers. Descriptive statistics, statistical tests, and data visualizations were developed for various indicators of dependence including cigarettes per day, time to first cigarette, Heaviness of Smoking Index (HSI), and Tobacco Dependence Index (TDI). The analyses were performed among the overall adult smoker population and by age groups (i.e., 18-24 and 25+ years of age).
Results: We observed higher level of dependence among non-menthol smokers compared to menthol smokers based on cigarettes per day (16.0 cigarettes for non-menthol smokers vs. 13.6 cigarettes for menthol cigarettes, $p<0.01$), percentage of smoking within 30 minutes after waking (60.2% vs. 56.2%, $p<0.01$), HSI (2.6 vs. 2.4, $p<0.01$), and TDI (55.0 vs. 51.2, $p<0.01$) among the overall adult smoker population. Similar

significant differences were also observed among adult smokers who were 25 years or older. No significant differences were found for various dependence indicators among young adults (18-24 years of age).
Conclusions: Our analyses of PATH dataset indicates that menthol cigarette smoking is not associated with increased cigarette dependence compared to non-menthol cigarette smoking. Conversely, we found a lower level of dependence among current adult menthol smokers. Further research (e.g., longitudinal or biomarker analyses) is needed to investigate the compelling evidence of the lack of associations between menthol smoking and dependence.
Financial Support: This work was funded by Altria Client Services LLC and all authors are employees of Altria Client Services LLC.

EXAMINING THE IMPACT OF E-CIGARETTE FLAVOR RESTRICTIONS ON E-CIGARETTE USE AND SUCCESS QUITTING SMOKING AMONG US ADULTS

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Drug Category Nicotine/Tobacco
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: The availability of flavored e-cigarettes is an important scientific and public health debate. Regulations have limited the availability of certain e-cigarette flavors to reduce the appeal and use of e-cigarettes among youth, yet it is unknown how these flavor restrictions impact adults who are using e-cigarettes to quit smoking cigarettes.
Methods: Online survey data were collected in October 2021 from 857 adults across the US who reported using e-cigarettes in a recent attempt to quit smoking. Survey items assessed what e-cigarette flavors were used during their quit attempt, whether e-cigarette flavor bans restricted access to flavors they like, and what impact the restrictions had on their e-cigarette behavior. Multivariable logistic regression models were used to examine the impact of flavor bans on success quitting smoking for 1 month or longer, including demographic covariates.
Results: 30.2% (N=259) reported restricted access to e-cigarette flavors they like. During their quit attempt, 64.9% (N=168) used tobacco or menthol flavored e-cigarettes, flavors not impacted by restrictions, and 90.7% (N=235) used another flavor that could be impacted; the most common were fruit, mint, and candy/dessert. The most common responses to flavor restrictions were switching devices to continue using preferred flavors (39.4%, N=102), using the same device but only with available flavors (35.9%, N=93), buying elsewhere (e.g., online) to obtain preferred flavors (19.3%, N=50), making one's own flavors (3.5%, N=9), and 'other' (e.g., no longer using e-cigarettes) (1.9%, N=5). However, the odds of quitting smoking for 1 month or longer were not significantly different between those experiencing flavor restrictions (vs. not), preferring tobacco/menthol (vs. restricted) flavor, or switching flavors in response to the bans (vs. finding another way to obtain restricted flavors) (ps>.14).
Conclusions: Flavor restrictions impacted e-cigarette use among adults using e-cigarettes to quit smoking but were not associated with success quitting smoking.
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DIFFERENCES IN FLAVORED CIGAR USE AMONG BLUNT AND NON-BLUNT CIGAR SMOKERS

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research

Aim: Flavored cigar products may appeal especially to youth and young adults who primarily use them for smoking blunts, where some or all the loose tobacco is replaced with cannabis. Our study aimed to identify the extent blunt smokers use flavored cigar products and which flavors they prefer.
Methods: We used data from Wave 4 (2017) Population Assessment of Tobacco and Health Study, a nationally representative cohort of US residents aged 12 or older. We analyzed youth and adults who smoked any type of cigar product (traditional, cigarillo, filtered) in the past year (n=9,967) and reported how often they smoked cigars as blunts. We examined whether their first cigar use was flavored, whether they smoked flavored cigars in the past month, and if so, the specific flavors used.
Results: We estimated that 36.7 million (14%) people in the US aged 12 or older smoked a cigar product in the past year, and of those, 25% smoked cigars only as blunts (blunt-only), 46% smoked cigars but never as blunts (cigar-only), and 29% smoked both cigars and blunts (dual). Blunt-only smokers were more likely to have used flavored cigars as their first cigar product used (OR=1.8) and in the past month (OR=3.0) compared to cigar-only smokers. Blunt-only smokers preferred fruit, chocolate, candy, or sweet flavors (for both first use and past-month outcomes), while cigar-only smokers preferred menthol, mint, clove, spice, and alcohol flavors.
Conclusions: Flavored cigar products, specifically fruit and other sweet flavors, appeal especially to youth and adults who smoke cigars as blunts and they may be involved with their initial and continued exposure to cigar products. These findings underscore the need to further study how bans on cigar flavors will affect different cigar consumers, particularly blunt smokers.
Financial Support: Research supported in part by a seed grant from the UAMS Vice Chancellor for Research and Innovation.

THE EFFECT OF FLAVOR RESTRICTIONS ON DEMAND FOR E-CIGARETTES IN E-CIGARETTE NAIVE SMOKERS

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Drug Category Nicotine/Tobacco
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: The present study used behavioral economic measures of demand to examine the impact of e-cigarette flavor restrictions (i.e., restricted flavors vs. unrestricted flavors) on the likelihood of e-cigarette uptake in e-cigarette naive current smokers. We hypothesized that demand for e-cigarettes measured using the unrestricted flavor task would be greater than demand assessed using the restricted flavor task.
Methods: 188 participants (e-cigarette-naive current smokers living in the US) were recruited using Amazon Mechanical Turk from August to October 2017. Participants completed a Qualtrics survey assessing demographic characteristics and current smoking patterns (e.g., FTCD). Participants then completed a novel probability-based hypothetical e-cigarette purchase task under two conditions: restricted flavors (e.g., only tobacco and menthol flavors available) and unrestricted flavors (all flavors available, including fruit and sweet desserts). In this task, participants reported the probability that they would try a disposable e-cigarette across a range of prices.
Results: Using Wilcoxon signed-rank tests, median breakpoint measures generated using restricted and unrestricted flavor hypothetical e-cigarette purchase tasks were not significantly different ($T = 880$, $p = .79$). However, median observed intensity of demand for e-cigarettes in the unrestricted flavor task were significantly higher than those observed in the restricted flavor task ($T = 143$, $p = .023$, small effect size $r = .11$).
Conclusions: Among e-cigarette naive current smokers, a novel probability-based hypothetical e-cigarette purchase task suggests that although flavors for pod-based e-cigarettes in the United States are currently restricted to tobacco and menthol, disposable and tank-based systems remain available in a broad range of flavors. The present findings suggest that restricting the available flavors of disposable e-cigarettes may reduce the likelihood of consumption of e-cigarettes.
Financial Support: National Institutes of Health grants P01CA200512 and R21DA046339

ORAL COMMUNICATION: CHOICE BEHAVIORS

ROLE OF UNCERTAIN DRUG COST ON CHOICE BETWEEN COCAINE OR FENTANYL VS. FOOD IN RHESUS MONKEYS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Relative to nondrug reinforcers, illicit drugs may be more uncertain in terms of their quality and in the time and effort required to obtain them. This uncertainty could contribute to excessive drug-seeking behavior at the expense of engaging in nondrug-related activities. We recently found that variable-ratio (VR) schedules of cocaine reinforcement increased the potency of cocaine to maintain choice over food compared with fixed-ratio (FR) schedules. We aimed to systematically replicate prior results using a different within-session dosing procedure with cocaine and fentanyl vs. food choice.
Methods: Adult male (n=3) rhesus monkeys chose between cocaine (0-0.03 mg/kg/injection) or fentanyl (0-1.0 µg/kg/injection) vs. food (2 pellets/delivery) under a 5-component, within-session dosing procedure. In different conditions, food was available under an FR 25, 50, or 100 schedule and drug was available under an FR or VR 100 schedule. Drug dose increased within session, across components.
Results: The potency of cocaine or fentanyl to maintain choice under an FR or VR schedule was an increasing function of the response requirement in effect for food and was generally greater under the VR compared with the FR schedule. The latter effect was not observed at relatively small food requirements (e.g., FR 25) but was observed under relatively costly food requirements (e.g., 50 or 100).
Conclusions: Our findings suggest that uncertain drug cost could contribute to excessive allocation of behavior towards illicit drugs at the expense of nondrug alternatives. Furthermore, the impact of uncertain drug cost on drug choice is lessened when nondrug reinforcers are relatively less costly. These results support the use of low-cost/high-magnitude reinforcers in behavioral treatments like contingency management and support the use of more predictable drug access through agonist-replacement therapy.
Financial Support: R01 DA045011 to S.L.H.

THE USE OF COCAINE-FOOD CHOICE PARADIGMS TO STUDY VULNERABILITY AND TREATMENT EFFICACY IN SOCIALLY HOUSED FEMALE AND MALE CYNOMOLGUS MONKEYS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The present studies cover two aspects of cocaine use disorder (CUD) in monkey models. Study 1: Approximately 17% of people that try cocaine will meet DSM criteria for CUD, so understanding the variables that mediate vulnerable is critical. We used a cocaine-food choice paradigm to model vulnerability. Study 2: An important consideration in evaluating potential treatments is that most individuals suffering from CUD also use tobacco products. For these studies, cocaine-experienced monkeys self-administered cocaine (saline, 0.001-0.1 mg/kg/inj) under a concurrent schedule with food pellets as the alternative reinforcer.
Methods: For acquisition (Study 1), monkeys were first trained to choose between 1- vs. 3-pellets under a concurrent fixed-ratio schedule. Saline and ascending doses of cocaine were made available for 3-5 consecutive sessions. In Study 2, non-reinforcing doses of nicotine (0.01-0.056 mg/kg/inj) were added to the cocaine solution and environmental manipulations were studied to determine whether the cocaine+nicotine combination was more resistant to changes than cocaine alone. We used a delay discounting procedure (Huskinson et al., 2015).
Results: Study 1: In 3 of 6 monkeys no dose of cocaine was preferred over food. However, after giving them access to cocaine under a fixed-ratio schedule and then re-introducing the choice paradigm, cocaine was preferred. Study 2: When a non-reinforcing dose of nicotine was added to a non-reinforcing cocaine

dose, cocaine were chosen (i.e., >80% drug choice) in 8 of the 10 monkeys. In delay discounting, the indifference point (IP; 50% choice between cocaine and food) was greater for the cocaine+nicotine combination compared with the cocaine alone choice.
Conclusions: Study 1: A history of cocaine access (without food), changed a "resilient" monkey. Study 2: Co-abuse of nicotine and cocaine can potentiate the reinforcing effects of cocaine and manipulations designed to decrease cocaine choice are less effective under conditions in which co-use of nicotine is studied.
Financial Support: NIDA DA017763-15

SEX DIFFERENCES IN THE EFFECT OF CHRONIC DELIVERY OF THE BUPRENORPHINE ANALOG BU08028 ON HEROIN RELAPSE AND CHOICE IN A RAT MODEL OF OPIOID MAINTENANCE

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Maintenance treatment with opioid agonists (buprenorphine, methadone) decreases opioid use and relapse. We recently modeled maintenance treatment in rats and found that chronic delivery of buprenorphine or the mu opioid receptor (MOR) partial agonist TRV130 decreases relapse to oxycodone seeking and taking. Here, we tested the effect of the buprenorphine analog BU08028 on different heroin relapse-related measures and heroin vs. food choice.
Methods: For relapse assessment, we trained male and female rats to self-administer heroin (6-h/d, 14-d) in context A and then implanted osmotic minipumps containing BU08028 (0, 0.03, or 0.1 mg/kg/d). We then tested the effect of chronic BU08028 delivery on (1) incubation of heroin seeking in a non-drug context B, (2) extinction responding reinforced by heroin-associated discrete cues in context B, (3) reinstatement of heroin seeking induced by re-exposure to context A, and (4) reacquisition of heroin self-administration in context A. For choice assessment, we tested the effect of chronic BU08028 delivery on heroin vs. food choice.
Results: Chronic BU08028 delivery decreased incubation of heroin seeking in both sexes and extinction responding in males only. Unexpectedly, BU08028 increased reacquisition of heroin self-administration selectively in females. Chronic BU08028 had minimal effects on context-induced reinstatement and heroin vs. food choice in both sexes.
Conclusions: Chronic BU08028 delivery had both beneficial and detrimental sex-dependent effects on different triggers of heroin relapse and had minimal effects on heroin choice in both sexes. Results suggest that BU08028 will not be an effective opioid maintenance treatment in humans.
Financial Support: This work was supported by NIDA/NIH and UG3DA050311
Synthesis of BU08028 was supported by the NIDA IRP Medication Development Program

ROLE OF PIRIFORM CORTEX AFFERENT PROJECTIONS IN RELAPSE TO FENTANYL SEEKING AFTER FOOD CHOICE-INDUCED VOLUNTARY ABSTINENCE

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: We previously showed a role of piriform cortex (Pir) in relapse to fentanyl seeking after food choice-induced voluntary abstinence, a procedure that mimics abstinence due to availability of alternative non-drug rewards. Here, we used retrograde tracing to determine projection-specific activation of Pir afferent projections during fentanyl relapse by using Fos plus the retrograde tracer cholera toxin B (injected into Pir).

Methods: We trained male and female rats to self-administer palatable food pellets for 6 days (6-h/day) and fentanyl (2.5 microgram/kg/infusion, i.v.) for 12 days (6-h/day). We assessed relapse to fentanyl seeking after 14 voluntary abstinence days, achieved through a discrete choice procedure between fentanyl and palatable food (20 trials/day).
Results: Relapse to fentanyl seeking was associated with increased Fos expression in neurons in anterior insular (AI) and prelimbic (PL) cortex that project to Pir but not Pir-projecting cortical neurons in adjacent areas or Pir-projecting thalamic neurons. Preliminary anterograde tracing in AI or PL confirmed these AI □ Pir and PL □ Pir projections.
Conclusions: Results demonstrate a correlational role of AI □ Pir and PL □ Pir projections in relapse to fentanyl seeking after food choice-induced abstinence. In future experiments, we will determine the causal role of these projections in relapse to fentanyl seeking after food choice-induced abstinence.
Financial Support: Funds to NIDA IRP, FI2GM128603 (DJR)

ORAL COMMUNICATION: **TRENDS IN POLYSUBSTANCE USE**

A NONHUMAN PRIMATE MODEL OF COCAINE/ALCOHOL CO-ABUSE: EFFECTS ON D2-LIKE AND D3 DOPAMINE RECEPTOR FUNCTION

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Estimates indicate that up to 90% of individuals with cocaine use disorder also co-abuse alcohol. However, little is known about the behavioral and neurobiological mechanisms that promote the co-abuse. For example, although studies in humans and laboratory animals have documented that chronic use of alcohol or cocaine can decrease dopamine D2-like receptor (D2R) availability and increase dopamine D3 receptor (D3R) function, effects of co-abuse of these substances has not been studied. Our laboratory has developed a nonhuman primate model of cocaine/alcohol co-abuse in which monkeys self-administer cocaine daily, with or without daily ethanol consumption.
Methods: Specifically, 12 adult male monkeys self-administered cocaine (0.1 mg/kg per injection) under a fixed ratio 30 schedule in the morning, five days per week. In the afternoon, six of these monkeys consumed 2.0 g/kg ethanol over one hour to model binge-like alcohol drinking and six monkeys drank a non-alcoholic solution. To measure D2R availability, positron emission tomography (PET) scans were performed using [11C]raclopride when monkeys were drug-naive and again after monkeys had self-administered approximately 400 mg/kg cocaine. To measure D3R function, the ability of the D3 receptor agonist quinpirole to elicit yawns was measured at the same time points.
Results: As seen previously, chronic cocaine self-administration decreased D2R availability, particularly in the putamen. However, this effect was not observed in monkeys who consumed ethanol. In contrast, sensitivity to quinpirole was increased in ethanol-drinking monkeys, whereas no systematic change was observed in the control group.
Conclusions: Results suggest that chronic alcohol drinking can modulate the effects of cocaine on brain dopamine function and that effects on D3R are more likely to be involved in promoting co-abuse than effects on D2R.
Financial Support: DA 039953

THE EFFECTS OF NALTREXONE AND BUPRENORPHINE ON SELF-ADMINISTRATION OF FENTANYL-ALPRAZOLAM COMBINATIONS IN RHESUS MONKEYS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Abstract Detail Animal Study

Abstract Category Original Research
Aim: Opioid-use disorder (OUD) is commonly associated with a high degree of benzodiazepine co-abuse. While FDA-approved treatments for OUD exist (i.e., methadone, naltrexone, buprenorphine), the effectiveness of these treatments at reducing opioid-benzodiazepine co-abuse is currently unknown. The objective of the present study was to evaluate the extent to which naltrexone and buprenorphine reduced i.v. self-administration of fentanyl and fentanyl-alprazolam combinations in rhesus monkeys.
Methods: Subjects were 6 (3m/3f) adult rhesus monkeys trained to self-administer remifentanil (0.0003 mg/kg/injection) under a progressive-ratio (PR) schedule of reinforcement. Test sessions were conducted within alternating remifentanil and saline baselines and evaluated the reinforcing effects of fentanyl (0.00056 mg/kg/injection for 5 animals and 0.0003 mg/kg/injection for 1 animal) and a combination of fentanyl and alprazolam following a pretreatment with naltrexone (0.0003 - 0.1 mg/kg; i.m), buprenorphine (0.003 - 0.3 mg/kg; i.m) or vehicle 10 minutes prior to the start of the session. Data were analyzed using one-way repeated-measures ANOVA and Bonferroni's multiple comparisons t-tests.
Results: All subjects self-administered fentanyl alone above vehicle levels. Additionally, four subjects self-administered the combination of fentanyl and alprazolam above vehicle levels. Both naltrexone ($p<0.0001$) and buprenorphine ($p<0.0001$) significantly blocked fentanyl self-administration, although the effective and ineffective doses for the pretreatments varied among the subjects. Naltrexone ($p<0.0001$) and buprenorphine ($p=0.0499$) significantly blocked self-administration of the fentanyl-alprazolam combination.
Conclusions: The current results suggest that naltrexone and buprenorphine, although showcasing individual variability, are effective treatments for reducing the reinforcing effects of opioid-benzodiazepine combinations in rhesus monkeys.
Financial Support: Funded by an ALKERMES PATHWAYS RESEARCH AWARDS® grant, an independent competitive grants program supported by Alkermes (to L.F.B.) and USPHS grant DA011792 (to J.K.R.).

COCAINE USE DURING OXYCODONE WITHDRAWAL REDUCES SOMATIC SIGNS OF WITHDRAWAL AND IS ASSOCIATED WITH ABERRANT ACCUMBENS GLUTAMATERGIC PLASTICITY

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Opioid use disorder (OUD) is a leading public health crisis in the United States. Individuals with OUD frequently use other substances, including cocaine. Mechanistically, glutamate signaling within corticostriatal circuitry has been shown to underlie the motivated use of both opioids and cocaine. Self-administration (SA) of these substances alters synaptic plasticity measured as changes in AMPA-to-NMDA current ratios (A/N) within the nucleus accumbens core (NAc), whereby cocaine potentiates A/N, and opioids induce long term depression (LTD) of NAc medium spiny neurons (MSNs). The current study determined whether cocaine use during oxycodone withdrawal (1) reduces somatic withdrawal signs, and (2) reverses oxycodone-induced LTD as measured by A/N.
Methods: Long Evans male/female rats (N=34) underwent oxycodone (0.03mg/kg/infusion,FR1) or food (FR1) and cocaine-SA (0.25mg/kg/infusion,FR1) in an A-B-A-B design. Rats underwent a minimum of 10-oxycodone-SA ("A") sessions prior to the first cocaine-SA ("B") phase, and following the second phase of oxycodone-SA, rats underwent one cocaine-SA session at the 24-hr oxycodone/food withdrawal time point followed by measurement of NAc A/N via slice-electrophysiology. Somatic signs of withdrawal were measured at 0,22, and 24 hrs post-oxycodone or food-SA.
Results: Cocaine consumption significantly increased following oxycodone withdrawal, ($p<0.01$, comparing cocaine consumption prior to and following 24 hr oxycodone withdrawal), but not following food SA ($p>0.05$). Further, cocaine SA significantly reduces somatic signs of oxycodone withdrawal ($p<0.05$), but did not significantly alter somatic signs in the food control group ($p>0.05$). Finally, NAcore A/N was decreased in the oxycodone/cocaine SA group as compared to the food/cocaine SA group, demonstrating LTD induced by oxycodone SA that is not reversed by cocaine.

Conclusions: Cocaine use during oxycodone SA reverses oxycodone withdrawal but does not reverse oxycodone-induced LTD in NAcore MSNs. Together, these data suggest that oxycodone use induces persistent changes in glutamatergic signaling, which may exacerbate motivation for cocaine co-use due to alleviation of withdrawal symptomatology.
Financial Support: NIDA

GENERAL PSYCHOPATHOLOGY FACTOR AS A MEDIATOR BETWEEN POLYSUBSTANCE USE AND DIMENSIONAL PSYCHOPATHOLOGY CONSTRUCTS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Research on the comorbidity of disorders suggests that broader, dimensional constructs of internalizing (INT; fear and distress), externalizing (EXT; antagonism), and thought disorder (TD) measures better underlie common mental health disorders. Shared variance across these dimensions has been noted, suggesting a broader general psychopathology factor (p-factor). Polysubstance use (PSU) is defined as the use of two or more addictive drugs simultaneously or concurrently and polysubstance use disorder (PSUD) is the presence of two or more substance use disorders (SUDs). Substance use is associated with broad increases across problem behaviors and psychopathology, and the current project assesses whether this is exacerbated by PSU. The goal of the project was to identify the relationship between PSU and dimensional psychopathology constructs (fear, distress, antagonism, TD, and p-Factor).
Methods: 2617 participants from a residential substance use treatment center in the DC area, serving primarily low-income, African American clients of both sexes, were recruited across 12 years. Structural equation modeling was used to develop the latent psychopathology and PSU factors and run mediation models. Analyses focused on the relationship between p-factor and PSU, and on p-factor's role in mediating the relationship between PSU and dimensional psychopathology constructs.
Results: Mediation models indicated that p-factor mediates the relationship between PSU and TD, and distress, but not for antagonism or fear. Antagonism remains significantly positive, but the relationship is weakened with p-factor as a mediator (from $r=.66$ to $r=.32$, $p<.01$). For fear, on the other hand, the relationship flipped from positive to negative (from $r=.76$ to $r=-.65$, $p<.01$).
Conclusions: Independently, there is a significant relationship between each dimensional psychopathology construct with PSU. However, when including p-factor as a mediator, PSU's weaker relationship with antagonism supports the view that antagonism is synergistic with SUDs, and PSU's resulting inverse relationship with fear suggests that p-factor may play a suppressor role relative to fear.
Financial Support: NIDA

MONDAY, JUNE 13, 2022

ORAL COMMUNICATION: SOCIAL ENVIRONMENT AND SUD BEHAVIORS

THE INFLUENCE OF SOCIAL CONTEXT ON MOOD DURING ALCOHOL CONSUMPTION IN YOUNG ADULTS

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research

Aim: Research frequently connects solitary drinking to negative affect reduction motives and social drinking to positive affect enhancement motives. Little research examines affect after drinking in varying social contexts, particularly in young adulthood where risk for problematic alcohol use is elevated. This study examined differences by social context in negative (NA) and positive affect (PA) during alcohol consumption. We hypothesized that NA and PA after drinking would vary as a function of social context (alone or with others).
Methods: 257 male and female young adults (M age = 21.3) completed 7 days of ecological momentary assessment assessing alcohol use, affect, and social context at two points of a longitudinal, observational study. Three-level mixed-effects location scale analyses examined effects of being alone vs. with others on PA and NA after drinking. Gender, study wave, and amount of alcohol consumed were covariates.
Results: PA was significantly lower when alone ($b = -.320$, $p < .001$), and higher after alcohol use ($b = .256$, $p < .001$). PA after alcohol use was diminished, however, when participants were alone, versus with others ($b = -.300$, $p = .004$). A significant interaction between alcohol use and social context demonstrated that NA was higher after solitary alcohol use, compared to times when alcohol was used with others ($b = .250$, $p = .010$).
Conclusions: Mood after alcohol use was dependent on social context: PA was elevated after drinking with others versus alone, and NA was higher after drinking alone versus with others. These findings demonstrate that solitary drinking, although frequently connected to negative affect reduction motives, may adversely result in greater NA. Additionally, increased PA after drinking with others suggests that social drinking is particularly reinforcing in young adulthood.
Financial Support: This research was supported by training grant T32AA026577 from NIH-NIAAA and grant 5P01CA098262 from the National Cancer Institute.

COCAINE-VS-SOCIAL CHOICE IN RATS IS SENSITIVE TO REINFORCER MAGNITUDE AND PRICE MANIPULATIONS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Cocaine use disorder occurs in an environmental context that includes both the abused drug and non-drug reinforcers, such as social interaction and relationships with family and friends. Accordingly, preclinical research has begun to incorporate social interaction into animal models of drug abuse. The goal of the present study was to determine the sensitivity of a cocaine-vs-social interaction choice self-administration procedure in male and female rats to reinforcer magnitude and response requirement (i.e., cost) manipulations.
Methods: Operant responding for social interaction with a conspecific rat and intravenous cocaine self-administration were initially trained separately in rats (n=8, 4 per sex). Subsequently, cocaine-vs-social interaction choice was determined at different cocaine doses (0 – 1.8 mg/kg/inf) in a discrete-trial choice procedure with equal fixed-ratio (FR3) requirements for both cocaine and social interaction. Next, rats were switched to a discrete-trial choice procedure where social interaction was held constant at FR3 and response requirement on the cocaine lever was a progressive-ratio (PR) schedule. Each dose condition was determined for 3-5 days. Data were analyzed using mixed-effects analysis of variance.
Results: Rats allocated behavior between cocaine and social interaction depending upon the unit cocaine dose. Rats chose social interaction over no or small cocaine doses (0, 0.032, 0.1 mg/kg/inf) under both the equal FR and PR discrete-trial choice procedures ($p<0.05$). Rats showed a decrease in cocaine choice between 0.32 mg/kg/inf cocaine and social interaction under the cocaine PR discrete-trial procedure compared to the equal FR procedure. However, rats chose larger cocaine doses (1 – 1.8 mg/kg/inf) over social interaction under both discrete-trial procedures ($p<0.05$).
Conclusions: The results demonstrate that cocaine-vs-social choice under a discrete-trial choice procedure is sensitive to reinforcer magnitude manipulations such as drug dose. Furthermore, these results provide an empirical foundation to test candidate medications for cocaine use disorder and investigate the neurobiology of drug-vs-social choice.
Financial Support: P30DA033934

SOCIAL DOMINANCE IN MONKEYS: EFFECTS OF LONG-TERM ETHANOL SELF-ADMINISTRATION

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Approximately 14.4 million adults in the US are diagnosed with alcohol use disorder (AUD). A lack of understanding of factors that confer vulnerability or resilience to developing AUD hinders the development of novel treatments. Although it is accepted that social stress perpetuates problematic drinking, the neurobiological mechanisms remain unknown. These mechanisms are difficult to identify in humans as it is nearly impossible to study subjects prior to alcohol exposure and polysubstance use and comorbid mental health diagnoses are common. Nonhuman primates are a useful laboratory model as they are the closest to humans in brain structure and function. Additionally, monkeys naturally form social dominance hierarchies which allow for examining the interaction between social variables and sensitivity to ethanol (EtOH).
Methods: In the present study, group-housed adult male cynomolgus monkeys lived in two stable social groups. Position in the social hierarchy reflects a continuum from environmental enrichment in dominant (DOM; n=4) monkeys to chronic social stress in subordinate (SUB; n=4) monkeys. Monkeys were trained to drink EtOH via an operant panel within the home-cage using well-established schedule-induction procedures. Monkeys then self-administered EtOH 22 hours/day, 4 days/week ("free access") for six months.
Results: Although rates and patterns of drinking did not differ between DOM and SUB monkeys during induction, intakes diverged upon the introduction of free access. SUBs maintained significantly greater mean weekly EtOH intakes (2.19 □ 0.99 g/kg) versus DOMs (0.37 □ 0.41; $p<0.05$). Moreover, intake increased in SUBs when a third pen experienced heightened aggression resulting in injuries and instability of the hierarchy (data not included).
Conclusions: Together, these data indicate that socially stressed SUB monkeys will consume more EtOH versus socially enriched DOM monkeys. This study is ongoing until one year of EtOH free access. At that time, novel pharmacological treatments will be assessed in monkeys with a range of drinking phenotypes.
Financial Support: NIH P50 AA 26117 and T32 AA 07565

CHARACTERIZATION OF OPERANT SOCIAL INTERACTION IN RATS: EFFECTS OF ACCESS DURATION, EFFORT, PEER FAMILIARITY, HOUSING CONDITIONS, AND CHOICE BETWEEN SOCIAL INTERACTION VS. FOOD OR REMIFENTANIL

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Social factors play a critical role in drug addiction. We recently showed that rats will abstain methamphetamine, cocaine, heroin, and remifentanil self-administration when given a choice between the addictive drug and operant social interaction. Here, we further characterized operant social interaction by determining the effects of access duration, effort, peer familiarity, and housing conditions. We also determined choice between social interaction vs. palatable food or remifentanil.
Methods: We first trained single-housed male (n=17) and female rats (n=32) to lever-press for social interaction with a sex-matched peer. Next, we determined effects of access duration (3.75 to 240 s), effort (increasing fixed ratio requirements or progressive ratio schedule), peer familiarity (familiar vs. unfamiliar), and housing conditions (single- vs. paired-housing) on social self-administration. We also determined choice between social interaction vs. palatable food pellets or intravenous remifentanil (0, 1, 10 μg/kg/infusion).

Results: Increasing access duration to a peer decreased social self-administration under FR but not progressive ratio schedule; the rats showed similar preference for short vs. long access duration. Social self-administration under different FR requirements was higher in single-housed than in paired-housed rats and higher for a familiar vs. unfamiliar partner in single-housed but not paired-housed rats. Response rates of food-sated rats under increasing FR requirements was significantly higher for palatable food than for social interaction. The rats strongly preferred palatable food over social interaction and showed dose-dependent preference for social interaction vs. remifentanil.
Conclusions: We identified parameters influencing the reinforcing effects of operant social interaction and introduce a choice procedure sensitive to remifentanil self-administration dose.
Financial Support: NIH/NIDA

ORAL COMMUNICATION: MACHINE LEARNING APPLICATIONS FOR SUDS

IDENTIFICATION OF SUBSTANCES USED IN SELF-MEDICATION OF OPIOID WITHDRAWAL: NATURAL LANGUAGE PROCESSING STUDY OF REDDIT DATA

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Drug Category Opiates/Opioids
Topic Artificial Intelligence
Abstract Detail Human
Abstract Category Original Research
Aim: To develop and validate methodology for identifying substances used to treat symptoms of opioid withdrawal by a community of people on the social media site Reddit.
Methods: We developed methodology and extracted substances and effects from nearly 4 million comments from the r/opiates and r/OpiatesRecovery subreddits. We focused on symptoms of opioid withdrawal and substances that are potential remedies for those symptoms. We built a bipartite network of substance and effect co-occurrence. For each of 16 effects identified as DSM-5 symptoms of opioid withdrawal, we identified the 10 most strongly associated substances. We developed the Withdrawal Remedy Explorer app to facilitate further exploration of the data.
Results: We identified 458 unique substances and 253 unique effects. Of 130 potential remedies strongly associated with withdrawal symptoms, 41.54% were FDA-approved or commonly utilized treatments for the symptom; 13.08% were not often used to treat the symptom but could be potentially useful given their pharmacological profile; 10.00% were natural/home remedies; 5.38% were causes of the symptom; and 30.00% were other/unclear. We identified both potentially promising remedies (e.g., gabapentin for body aches) and potentially common but harmful remedies (e.g., antihistamines for restless leg syndrome).
Conclusions: Social media is a promising source of data on self-medication of opioid withdrawal. Many of the withdrawal remedies discussed by Reddit users are either clinically proven or potentially useful. These results suggest that this methodology is a valid way to study the self-treatment behavior of an online community of people who use opioids. Our Withdrawal Remedy Explorer application provides a platform to use these data for pharmacovigilance, identification of new treatments, and better understanding the needs of people undergoing opioid withdrawal. Furthermore, this approach could be applied to many other disease states where people self-manage their symptoms and discuss their experiences online.
Financial Support: Funded by NIDA grant 5R21DA048739-02

USING PUBLICLY AVAILABLE DATA TO PREDICT RECREATIONAL CANNABIS LEGALIZATION AT THE COUNTY-LEVEL: A MACHINE LEARNING APPROACH

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Drug Category Cannabis/Cannabinoids
Topic Artificial Intelligence
Abstract Detail Human
Abstract Category Original Research
Aim: There is substantial geographic variability in local cannabis policies within states that have legalized recreational cannabis. This study develops an interpretable machine learning model that uses county-level

population demographics, sociopolitical factors, and estimates of substance use and mental illness prevalences to predict the legalization of county-level recreational cannabis sale.
Methods: Data from the 2010 Census, 2012 County Presidential Data from the MIT Elections Lab, and Small Area Estimates from the National Surveys on Drug Use and Health (NSDUH) from 2010 to 2012 were merged at the county level. We built an interpretable machine learning model by stacking an ensemble of logistic regressions fit to random realizations of the observed data. County-level predictions were obtained as a weighted average of predictions from each logistic model, with model-averaging weights based on model accuracy. Predictive performance was evaluated by comparing 2014 predictions to actual outcomes and calculating area under the curve (AUC), accuracy, sensitivity, and specificity. Optimal cut-point was varied to either minimize the false positive (Type I) or false negative (Type II) rate.
Results: Our model-averaging predictions had an AUC of 0.95, 90-95% accuracy, 96-100% sensitivity, and 90-92% specificity, depending on the cut-point and the goal of either minimizing the Type I or the Type II error rate. The main factors associated with county-level variations in support of recreational cannabis law were land area of the county, and the prevalences of past year serious mental illness, past month cannabis use, and past year cocaine use.
Conclusions: We show that, by leveraging publicly available data from the period 2010-2012, our model was able to achieve high levels of discrimination in predicting which counties would legalize recreational cannabis sales in 2014. Having demonstrated model performance, this set of covariates can be used as a valid set of controls in modelling differences between counties after legalization.

PREDICTING COUNTY-LEVEL OVERDOSE DEATH RATES AMID THE ESCALATING OVERDOSE CRISIS IN THE UNITED STATES: A STATISTICAL MODELING APPROACH PREDICTING DEATHS THROUGH 2022

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Drug Category Opiates/Opioids
Topic Artificial Intelligence
Abstract Detail Human
Abstract Category Original Research
Aim: U.S. overdose (OD) deaths continue to escalate but are characterized by geographic and temporal heterogeneity. We previously validated a predictive statistical model to predict county-level OD mortality nationally from 2013 to 2018. Herein, we aimed to: 1) validate our model's performance at predicting county-level OD mortality in 2019 and 2020; 2) modify and validate our model to predict OD mortality in 2022.
Methods: We evaluated our mixed effects negative binomial model's performance at predicting county-level OD mortality in 2019 and 2020. Further, we modified our model which originally used data from the year X to predict OD deaths in the year X+1 to instead predict deaths in year X+3. We validated this modification for the years 2017 through 2019 and generated future-oriented predictions for 2022. Finally, to leverage available, albeit incomplete, 2020 OD mortality data, we also modified and validated our model to predict OD deaths in year X+2 and generated an alternative set of predictions for 2022.
Results: Our original model continued to perform with similar efficacy in 2019 and 2020, remaining superior to a benchmark approach. Our modified X+3 model performed with similar efficacy as our original model, and we present predictions for 2022, including identification of counties most likely to experience highest OD mortality rates. There was a high correlation (Spearman's $\rho = 0.93$) between the rank ordering of counties for our 2022 predictions using our X+3 and X+2 models. However, the X+3 model (which did not account for OD escalation during COVID) predicted only 62,000 deaths nationwide for 2022, whereas the X+2 model predicted over 87,000.
Conclusions: We have predicted county-level overdose death rates for 2022 across the US. These predictions, made publicly available in our online application, can be used to identify counties at highest risk of high OD mortality and support evidence-based OD prevention planning.
Financial Support: This study was supported by a National Institute on Drug Abuse Avenir grant (DP2DA049295).

ORAL COMMUNICATION: METHAMPHETAMINE, BASIC SCIENCE

HIV-1 TAT PROTEIN EXACERBATES METHAMPHETAMINE-DYSREGULATED DOPAMINE UPTAKE INTO VESICULAR MONOAMINE TRANSPORTER-2 AND POTENTIATES METHAMPHETAMINE CONDITIONED PLACE PREFERENCE IN HIV-1 TAT TRANSGENIC MICE

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Drug Category Stimulants
Topic Molecular Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Methamphetamine (METH) abuse has been shown to increase the incidence of HIV-1 associated neurocognitive disorders (HAND). We have demonstrated that the HIV-1 regulatory protein, transactivator of transcription (Tat), decreases dopamine (DA) transport via the DA transporter (DAT) and vesicular monoamine transporter-2 (VMAT-2). This study examined the synergistic effects of Tat and METH on DA uptake through VMAT-2 and associated METH-induced conditioned place preference.
Methods: Vesicular [3H]dopamine uptake into isolated whole mouse brain vesicles of HIV-1 Tat transgenic mice and methamphetamine-induced conditioned place preference.
Results: In vitro incubation of isolated mouse whole brain vesicles with recombinant Tat1-86 or METH displayed a concentration-dependent inhibition of vesicular [3H]DA uptake, in which a combination of Tat and METH induced an additive reduction of DA uptake via VMAT-2 compared to Tat or METH alone. 21-day doxycycline (Dox, 100 mg/kg/day, i.p.)-induced Tat expression caused a 57% decrease in the maximal velocity (Vmax) value in inducible Tat transgenic (iTat-tg) mice, which was attenuated in control G-tg (Tat null) mice. 14-day administration of METH (3 mg/kg, i.p.) alone induced a 35% and 52% reduction of Vmax in iTat-tg and G-tg mice, respectively, whereas a greater decrease (66%) in Vmax was observed in iTat-tg mice of Dox-METH group. Following 14-day treatment of Dox, the iTat-tg mice potentiated METH-CPP 6-fold over saline-treated mice, suggesting that Tat expression potentiates the rewarding effect of METH.
Conclusions: Considering that both Tat and METH interact with DAT and VMAT-2, these results provide evidence that Tat and METH could disrupt DA transmission by inhibiting both DAT and VMAT-2 function. This study raises the exciting possibility of a potential therapeutic strategy by targeting VMAT-2 for METH abuse in HIV infected individuals.
Financial Support: NIH grant DA035714 and DA041932

CORTICAL THICKNESS AND RELATED DEPRESSIVE SYMPTOMS IN EARLY ABSTINENCE FROM CHRONIC METHAMPHETAMINE MISUSE

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: People diagnosed with Methamphetamine Use Disorder (MUD) often approach a treatment episode during early abstinence from methamphetamine, when depressive symptoms promote relapse. The goal of this study was to identify neural correlates of these symptoms, possibly revealing targets for intervention. We hypothesized that smaller cortical thickness would be related to self-reports of greater depressive symptoms during early abstinence from chronic methamphetamine misuse.
Methods: The sample comprised 34 women and 55 men with MUD in early abstinence (M±SD=22.1±25.6 days) who reported depressive symptoms on the Beck Depression Inventory (BDI) and 89 healthy controls. The two groups were well-matched on age, sex, and recent use of alcohol, tobacco, and marijuana. Thickness across the cerebral cortex was analyzed using FreeSurfer software, fitting a general linear model to identify differences between groups. To determine whether cortical thickness in regions showing group

differences were related to depressive symptoms in early abstinence from methamphetamine, follow-up regressions were performed in SPSS.
Results: The MUD group exhibited smaller thickness in clusters within bilateral frontal, parietal, temporal, insular, and right cingulate cortices relative to healthy controls (all cluster ps<0.05, corrected for multiple comparisons). Depressive symptoms in the MUD group (BDI score, M±SD=8.7±8.6) were positively correlated with cortical thickness in the regions exhibiting less gray matter in MUD versus healthy controls (β=0.263, p=0.017). These regions included the right anterior cingulate cortex (β=0.242, p=0.031).
Conclusions: Early abstinence from chronic methamphetamine misuse features widespread cortical deficits, particularly in the right anterior cingulate cortex, these deficits being associated with severity of depressive symptoms. Noninvasive stimulation of the anterior cingulate may offer a precise intervention for reducing depressive symptoms and relapse to methamphetamine use. Just as anterior cingulate pathology in Major Depressive Disorder predicts response to antidepressants, cingulate structure may also identify patients with MUD who can benefit from antidepressant medication.
Financial Support: Supported by grants from the National Institute on Drug Abuse (R01 DA027633) and the National Institutes of Health (K23 DA927734, R21 DA034928 (AD); R01 DA015179, R01 DA020726, P20 DA022539 (EL)). Additional funding provided by UL1TR000124 (UCLA CTSI), the Thomas P. and Katherine K. Pike Chair of Addiction Studies (EL), the Marjorie M. Greene Trust (EL), and a postdoctoral research grant from the Max Kade Foundation (JP).

NEURAL CORRELATES OF SEX DIFFERENCES IN SELF-REPORT IMPULSIVITY OF RESEARCH PARTICIPANTS WITH METHAMPHETAMINE USE DISORDER IN EARLY ABSTINENCE

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Early abstinence is a critical period when clients with Methamphetamine Use Disorder (MUD) approach a treatment episode. Knowledge of how the brain differs from controls at this time and how differences link to addiction-related behaviors may guide development of treatments. We hypothesized MUD individuals would have reduced cortical and subcortical volumes and these effects would be greater in female MUD individuals.
Methods: 218 individuals with MUD (131 male, 87 female, 18-57 years old) were recruited for participation after 4-7 days of abstinence from methamphetamine. Also recruited were matched healthy adult controls (193 male, 139 female). All participants completed the Barratt Impulsiveness Scale (BIS). A subset of participants (105 MUD, 118 Control, balanced for sex) received structural MRI scans. All scans were segmented using FreeSurfer, and regions of interest, including the superior frontal cortex, orbitofrontal cortex (OFC), and striatum, were identified. Subcortical and cortical volumes were extracted, and cortical thickness was determined.
Results: BIS scores were higher in the MUD group (p<0.001), more so in female participants (interaction: p=0.002). Males had larger cortical volumes in the left superior frontal cortex (p<0.001) and right medial OFC (p=0.04), but MUD males had smaller cortical volumes relative to control males (Superior Frontal: p=0.046, medial OFC: p=0.04). Caudate volumes were smaller in the MUD vs. the control group (p=0.018), and in males vs. females (p=0.03), but there were no interactions. Though significant brain effects were lateralized, similar trend-level effects were observed in the contralateral hemisphere. Finally, left medial OFC thickness correlated with BIS (p=0.01), more so in females (trend interaction p=0.07).
Conclusions: Sex-specific differences in brain structure and impulsivity during early abstinence may support individualized treatment plans for MUD. Negative association of medial OFC thickness with impulsivity in all subjects suggests this region may regulate impulsive behavior.
Financial Support: Supported by grants from the National Institute on Drug Abuse (R01 DA027633 (EDL), R01DA045162 (EDL), R01 DA020726 (EDL), P20 DA022539 (EDL), K23 DA927734 and R21 DA034928 (ACD), DA045162 (EDL), 5F32DA047111 (MNM). Additional funding provided by

UL1TR000124 (UCLA CTSI), the Thomas P. and Katherine K. Pike Chair of Addiction Studies (EDL), the Marjorie M. Greene Trust (EDL).

DECONSTRUCTING RISKY DECISION-MAKING IN METHAMPHETAMINE USE DISORDER: BEHAVIORAL UPDATING AND ITS NEURAL CORRELATES

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Although overdose deaths from methamphetamine misuse in the United States have nearly tripled from 2015 to 2019, no FDA-approved medication for Methamphetamine Use Disorder (MUD) exists. Behavioral treatments are the mainstay but their development is stymied by an imprecise understanding of the relevant behavioral problems. The goal of this study was to clarify the basis of disadvantageous decision-making by people with MUD.
Methods: Thirty participants with MUD and 69 healthy controls performed the Balloon Analogue Risk Task (BART), a laboratory test that simulates real-world decision-making under uncertainty and on which people with MUD make disadvantageous choices. A computational model was used to deconstruct behavior into risk-taking and behavioral updating, a measure of outcome-dependent changes in responding during task performance. A sample of 30 MUD and 69 control participants performed the BART during functional magnetic resonance imaging, and a separate sample of 28 MUD and 16 control participants underwent [18F]fallypride positron emission tomography scans to measure dopamine D2-type receptor availability (BPND) in the midbrain, striatum, insula, and medial and lateral orbitofrontal cortex.
Results: Participants with MUD took less risk, earned less reward, and exhibited slower behavioral updating than controls. Across groups, behavioral updating was correlated with modulation of activation in the dorsolateral prefrontal cortex and anterior insula during risk-taking. Only the healthy control group showed a negative correlation between risk-taking and D2-type BPND in the striatum and midbrain. They also showed quadratic associations between updating rate and D2-type BPND in the insula and medial orbitofrontal cortex.
Conclusions: These findings identify behavioral updating as a factor in maladaptive decision-making under uncertainty in MUD and suggest that dysregulation of D2-signaling in striatal and cortical regions and potentially disrupted activation of key prefrontal cortical regions underlying decision making contribute to maladaptive risky decision-making in MUD.
Financial Support: R01DA045162; 5F32DA047111; 1F31DA047110; 5T32DA024635

ORAL COMMUNICATION: ECOLOGICAL MOMENTARY ASSESSMENT INNOVATIONS

REMOTE DATA APPROACHES FOR EVALUATING THE THERAPEUTIC AND IMPAIRING EFFECTS OF CANNABIS IN REAL-WORLD SETTINGS

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Drug Category Cannabis/Cannabinoids
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: Access to medicinal cannabis is expanding rapidly; yet little controlled data exist on therapeutic efficacy and how variations in cannabinoid composition alter the balance between medicinal benefit and performance impairment. Participants in this study (N=25; 64% female) prospectively completed assessments of mood, sleep, cannabis use, and subjective feelings of impairment using a phone application immediately before and for 8 weeks after newly initiating medicinal cannabis use.
Methods: Access to medicinal cannabis is expanding rapidly; yet little controlled data exist on therapeutic efficacy and how variations in cannabinoid composition alter the balance between medicinal benefit and

performance impairment. Participants in this study (N=25; 64% female) prospectively completed assessments of mood, sleep, cannabis use, and subjective feelings of impairment using a phone application immediately before and for 8 weeks after newly initiating medicinal cannabis use.
Results: Reductions in anxiety and depressive symptoms were observed post-administration that were similar across routes of administration, $p < .05$. Impairment (e.g., subjective high, perceived driving impairment) was detected and differed by route of administration and gender, with less impairment reported with oral administration and among women. Evaluation of dose effects showed greater decreases in perceived driving ability and increases in subjective high when higher THC doses were administered, but no differences by CBD dose, $p < .05$.
Conclusions: Reductions in anxiety and depressive symptoms were observed post-administration that were similar across routes of administration, $p < .05$. Impairment (e.g., subjective high, perceived driving impairment) was detected and differed by route of administration and gender, with less impairment reported with oral administration and among women. Evaluation of dose effects showed greater decreases in perceived driving ability and increases in subjective high when higher THC doses were administered, but no differences by CBD dose, $p < .05$.
Financial Support: Pilot Research Funds from Thomas Jefferson University

USING AN ECOLOGICAL MOMENTARY ASSESSMENT METHODOLOGY TO ASSESS THE ACCURACY OF DAILY SURVEYS IN DETECTING DRINKING EVENT START TIME AND BINGE AND HEAVY ALCOHOL DRINKING PATTERNS

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Drug Category Alcohol
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Retrospective alcohol use data collection is prone to recall bias, a limitation that could be addressed with real-time ecological momentary assessment (EMA) tools. We aimed to 1) introduce a simple (single-click) EMA methodology for collecting real-time alcohol use data, 2) investigate daily survey performance in identifying drinking event start time and in detecting excessive alcohol drinking relative to the real-time data.
Methods: In March-April 2021, we sampled undergraduate students (N=84, n female=59, n male=25) and collected a week of alcohol use data. Participants entered their real-time drinking start time using our EMA methodology and self-reported their drinking details in daily surveys. We calculated the absolute time difference between drinking start times in the daily surveys and EMA data and estimated the accuracy of daily surveys in detecting binge/heavy drinking.
Results: Overall, 213 drinking days were reported in daily surveys. The median absolute time difference between the EMA data and daily survey was 16 minutes (IQR: 33 minutes). Number of drinks self-reported in daily surveys were correlated with that in the EMA data (r=.82, p=1e-46) and with the BAC readings (r=.62, p=2e-06). Sensitivity and specificity of daily surveys in detecting heavy drinking were, 97% (95% CI: 86%-100%) and 83% (95% CI: 69%-92%), respectively. These were 89% (95% CI: 80%-95%) and 80% (95% CI: 71%-87%) for binge drinking.
Conclusions: We developed a successful EMA methodology for collecting real-time alcohol use data. Further, our findings support the utility of drinking daily surveys in detecting drinking event start time, binge drinking, and heavy drinking.
Financial Support: This work was supported by the National Institute on Alcohol Abuse and Alcoholism [NIAAA grant # R25DA051249, 2021] and Prevention Insights at the Indiana University Bloomington School of Public Health. NIAAA had no role in the design, analysis, interpretation, or publication of this study. The content is solely the responsibility of the authors.

SLEEP DURING HCV TREATMENT IN PEOPLE WHO USE OPIOIDS: ASSESSMENT BY DAILY ELECTRONIC DIARY

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: People with hepatitis C virus (HCV) infection frequently report sleep problems and fatigue. HCV treatment and virologic cure (i.e., sustained virologic response, SVR) can improve sleep. Opioid use can also disrupt sleep. Here, we characterized by daily electronic diary the sleep of people with HCV and opioid misuse during and after direct acting antiviral (DAA) treatment.
Methods: 54 outpatients (22 female, 32 male) with chronic HCV and opioid misuse received standard-of-care DAA treatment for 8-12 weeks with SVR determined at 12 weeks post-treatment. Throughout these 24 weeks, participants provided ecological momentary assessment data using study-issued smartphones. Previous night's sleep was assessed in an "end-of-day" questionnaire issued each day 15-30 min before participants' typical bedtime. Differences by SVR (n = 39 SVRYes, 15 SVRNo/Unknown) were analyzed with (generalized) linear mixed models.
Results: Both SVRYes and SVRNo/Unknown participants reported unhealthy short (i.e., < 7 h) sleep durations that did not differ by group: (mean [SEM]) 4.8 (0.5) hours for SVRYes and 5.5 (0.8) hours for SVRNo/Unknown. Participants' reports of getting enough sleep and of feeling rested were endorsed in slightly less than half of responses and did not differ by group. SVRYes participants were more likely to report sleeping in a safe location and, in the 12 post-treatment weeks before SVR determination, a comfortable location. Consistent with these differences, SVRYes participants most frequently reported sleeping at their own house (44.3% of responses), whereas SVRNo/Unknown participants most frequently reported sleeping on the street (33.9% of responses).
Conclusions: Both SVRYes and SVRNo/Unknown participants experienced sleep problems: short durations and poor quality (i.e., not restful) sleep. Unlike previous studies not focused on people who use opioids, we did not find improved sleep in SVRYes participants. More work is needed to understand how opioid use may interact with HCV and its treatment to impact sleep.
Financial Support: NIH Office of AIDS Research (HHSN269201400012C); Merck and Co., Inc. (investigator-initiated grant, drug donation); NIDA Intramural Research Program

CANCOPE: ENGAGEMENT WITH AND ACCEPTABILITY OF A DIGITAL INTERVENTION FOR CANNABIS CRAVING

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Drug Category Cannabis/Cannabinoids
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: To develop and test an ecological momentary intervention (EMI) for cannabis craving in young adults. This pilot microrandomized trial compared mindfulness and distraction strategies for reducing momentary cannabis craving
Methods: Young adults (19–25 years; male and female) who responded to a social media ad targeting those thinking about reducing their cannabis use and who reported using cannabis >10 of the past 30 days participated in the 4-week intervention (n=55). Ecological momentary assessments (EMA) were delivered via smartphone app 5x/day. Participants earned $1/EMA, + $10/week for completing >80% of EMAs. Only those who completed >1 EMA were analyzed (N=53). Participants who reported craving >4/10 on any EMA were microrandomized to receive a mindfulness or a distraction coping strategy or a thank you message. Post-intervention, participants rated app satisfaction, ease of use, burden, and usefulness on a 7-point scale.
Results: On average, participants completed 64% of the EMAs during the four-week program, with stable responding across all 4 weeks (>60% completed each week). 81% of participants completed >50% EMA in week four of the intervention. In general, participants found the app easy to use (mean = 5.7, SD = 1.3), were satisfied with the app (mean = 5.0, SD = 1.5), and rated the app burden low (mean = 2.5, SD = 1.4).

Lowest scores were obtained on app usefulness (mean = 4.0, SD = 1.2). Participants also provided written feedback about the app that will be summarized in the presentation.
Conclusions: This study provides early support for the feasibility and acceptability of a mobile intervention to help young adults cope with cannabis cravings as they try to reduce their use. This engagement data will be used in combination with results for the effects of each message type to refine this intervention for further testing.
Financial Support: NIDA Technology-based Treatments for Substance Use Disorders P30DA029926; NIDA Training in the Science of Co-Occurring Disorders T32DA037202

ORAL COMMUNICATION: GENETICS OF SUDS I

MU-OPIOID RECEPTOR EPIGENETICS IN PERSONS WITH OPIOID USE DISORDER: A PILOT STUDY

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Drug Category Opiates/Opioids
Topic Genetics/Proteomics/Metabalomics
Abstract Detail Human
Abstract Category Original Research
Aim: DNA methylation markers may estimate chronological age with predictive value for frailty and mortality, and recent evidence suggests certain stressors may accelerate biological aging. DNA methylation of μ-opioid receptors is a potential experience-dependent marker of opioid use effects and treatment outcomes. This pilot study investigated in persons with opioid use disorder (OUD) whether μ-receptor epigenetic variation relates to pre-experimental factors and experimental buprenorphine/naloxone (B/N) stabilization dose (relative to morphine).
Methods: Non-treatment seeking volunteers with OUD provided whole-blood samples, assessed for DNA methylation using Infinium EPIC whole-genome array with probes at 64 μ-receptor sites. Epigenetic and phenotype data (demographics, drug use, and Adverse Childhood Experiences [ACE-IQ]) were available at screening for 20 participants (ages 26-57). Nine of these participants completed a within-subject crossover study, starting with 2 days of oral morphine stabilization (tailored to pre-experimental opioid use; range, 30–75 mg TID), followed by randomized, blinded exposure for 2 weeks each to low, moderate, and high daily doses of sublingual B/N (1.4/0.36, 4.2/1.08, and 12.8/3.2 mg Zubsolv™) and provided epigenetic and symptom data in each medication condition.
Results: At baseline (during morphine), median DNA methylation (normalized beta values, range: 0-1) across the 64 μ-receptor sites was 0.81 (range, 0.082–0.946). Using Spearman rho correlations (exploratory threshold $p<.01$), methylation values significantly related to subject's age (10 μ-receptor sites), current daily heroin-use amount (5 sites), and whether the subject's parents had separated/divorced (8 sites). B/N doses (relative to morphine) did not produce a biologically reliable influence (<5% variation) on average methylation values at any μ-receptor site, thus, correlations with symptoms were not undertaken.
Conclusions: Although sample size is small, these preliminary data suggest μ-receptor DNA methylation appears related to age (senescence clock), current heroin use, and parental divorce/separation (but not other early-life stressors), whereas short-term stabilization on different doses of B/N does not affect μ-receptor methylation.
Financial Support: NIH R01 DA015462 (methylation analysis conducted by WSU Genome Sciences Center), Gertrude Levin Endowed Chair in Addiction and Pain Biology (MG), NIH F30 DA052118 (TM), Lycaki/Young Funds (State of Michigan) and Detroit Wayne Integrated Health Network.

SPECIFICITY OF GENETIC AND ENVIRONMENTAL RISK FACTORS FOR PRESCRIPTION OPIOID MISUSE AND HEROIN USE

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Drug Category Opiates/Opioids
Topic Epidemiology

Abstract Detail Human
Abstract Category Original Research
Aim: To explore whether prescription opioid misuse (POM) is more etiologically similar to other prescription misuse, and whether heroin use is more etiologically similar to other illicit drug use, using multivariate twin modeling.
Methods: 2,663 same-sex pairs from the Australian Twin Registry (56% women; mean age=29.9 years) reported the number of times they misused prescription opioids, stimulants, and sedatives, and used heroin, cannabis, cocaine, methamphetamine, ecstasy/MDMA, hallucinogens, inhalants, solvents, and dissociatives in their lifetime. Independent pathway models were run: a full model containing 3 genetic (A), 3 shared environmental (C), and 3 unique environmental factors (E) common to all drugs, and drug-specific influences; a full model parameterized with a bifactor structure to accommodate a common factor reflecting general liability for all drug use, a prescription misuse factor, and an illicit drug use factor for each A, C, and E; and reduced models. Model comparison was conducted using chi-square likelihood ratio tests.
Results: POM and heroin use did not differentially associate with prescription misuse and illicit use, respectively, and the bifactor configuration provided poorer fit to the data than did the full model that allowed all drugs to freely cross-load on all factors [$\chi2(36)=1{,}166.39$, $p<.001$]. A common C factor and all drug-specific C factors could be dropped [$\chi2(24)=13.93$, $p=.95$]. A bifactor configuration of this simplified model also deteriorated model fit [$\chi2(22)=2{,}940.20$, $p<.001$]. There was evidence for drug-specific variance in POM (19%), but not heroin use. 74% and 79% of the respective variance in POM and heroin use loaded on a single common E factor, which was shared to a modest degree with prescription sedative misuse and methamphetamine use.
Conclusions: POM and heroin use appear to be driven by unique environmental influences, which may be largely overlapping. This is consistent with past findings demonstrating limited evidence for shared genetic etiology between these phenotypes.
Financial Support: F31DA054701

INTEGRATING BRAIN IMAGING PHENOTYPES, GENOMICS, AND SUBSTANCE USE

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Cigarette smoking is associated with persistent neurochemical and pathological changes in the brain. Recently UK Biobank retrieved MRI data from healthy individuals which allows for the opportunity to identify pre-symptomatic markers for neuropathological conditions associated with smoking behaviors. This study aims to establish a link between genetics, brain, and smoking behavior using this dataset.
Methods: Using the subset of UK Biobank data of 18,988 individuals, we first studied the association between cigarette smoking and brain imaging-derived phenotypes (IDPs). We used a total of 930 IDPs (474 structural and 420 diffusion MRI-derived phenotypes and 6 resting-state IDP groups). Individuals were divided into 1) Current daily smoking group (n=783), former daily smoking (n=4,250), those who smoked less than 100 cigarettes (n=3,290), and never smoked (n=8,114). We performed regression analyses to measure the association between 930 IDPs and 1) smoking status and 2) pack years. Then we created smoking-related polygenic risk scores (PRSs) using summary statistics from GWAS and Sequencing Consortium of Alcohol and Nicotine use. After assessing its predictive ability for UK Biobank smoking phenotypes, we performed regression analyses to observe the association between PRSs and IDPs.
Results: Ever daily smoking (compared to non or never smoked) had a strong association with 239 of 930 IDPs (82 structural, 156 diffusion, 1 resting-state group). The brain regions most significantly associated were putamen, caudate, pallidum for both hemispheres. For diffusion tracts, fornix, corona radiata, and longitudinal fasciculus were most significantly associated with the adverse direction of effect (decreased white matter integrity). The dose-effect of smoking (pack-years) generally showed that a higher dose of cigarettes was associated with decreased brain volume and white matter integrity. PRS showed no significant association.
Conclusions: Daily smoking results in widespread pathologic changes in the brain, and these changes are the result of smoking and do not represent genetic predisposition to smoking behaviors.

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GENETIC EVIDENCE FOR CANNABIS USE DISORDER (CUD) SEVERITY IN TWO HIGH-RISK POPULATIONS

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Drug Category Cannabis/Cannabinoids
Topic Genetics/Proteomics/Metabalomics
Abstract Detail Human
Abstract Category Original Research
Aim: Large disparities exist in CUD prevalence among different ethnic groups in the U.S., with American Indians exhibiting the highest rates and most severe levels of CUD. This work is part of a larger study exploring risk factors for substance use disorders in high-risk populations, and aimed to conduct genome-wide association analysis, gene-based analysis, and pleiotropic detection on a CUD-severity phenotype in an American Indian (AI) and a Mexican American (MA) populations.
Methods: 742 AI and 546 MA participants were assessed using the Semi-Structured-Assessment-for-the-Genetics-of-Alcoholism (SSAGA). We defined a quantitative CUD-severity phenotype for the clinical course of CUD that ranked 20 cannabis-related life-events from the SSAGA. AI had low-coverage whole genome sequences; MA had exome genotypes. Association analyses and gene-based burden tests were performed on CUD-severity. Linear mixed model (LMM) was employed to control for admixture and relatedness. Regularized regression lasso with LMM was used for pleiotropy detection to select the best sets of SNPs from the GWAS catalog for CUD-severity in AI and MA. The top findings were subjected to functional/pathway analyses.
Results: 11 variants from AI and 2 from MA were significantly associated with CUD-severity ($p<5E-8$). Genes associated with top variants from AI were enriched in regulation of dendrite development. The top genes from gene-based tests were enriched in several immunological signatures for AI, and oligodendrocyte differentiation, extracellular vesicles in the crosstalk of cardiac cells, and methylation pathways in MA, with breast cancer amplicon enriched in both cohorts. We further identified 150 and 188 pleiotropic variants from the GWAS catalog for CUD-severity in AI and MA respectively. Of the traits associated with the selected variants, PHF-tau measurement (a biomarker for Alzheimer's disease) is enriched in both cohorts.
Conclusions: Taken together, the study suggests that the AI and MA populations may have both shared and distinct pathways associated with CUD-severity.
Financial Support: Supported by DP1DA054373, K25AA025095, R01AA027316, R01AA026248, R01DA030976

ORAL COMMUNICATION: NEUROSCIENCE OF SUDS I

IN VIVO PHARMACOLOGICAL EFFECTS OF 5-MEO-MIPT AND ITS ANALOGS AT 5-HT2A AND 5-HT1A RECEPTORS IN MICE

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Drug Category Club/Designer Drugs
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: 5-methoxy-N-methyl-N-isopropyl-tryptamine (5-MeO-MiPT) is an analog of the Schedule I controlled psychedelic substance, 5-methoxy-N,N-dimethyltrytpamine (5-MeO-DMT). 5-MeO-MiPT is being sold as a "legal" alternative to classic psychedelic compounds, but little is known about its pharmacology. Here we investigated the in vivo effects of 5-MeO-MiPT, its dialkyl analog 5-methoxy-N,N-diisopropyltrytpamine (5-MeO-DiPT), and its O-demethylated metabolite 5-methoxy-N-isopropryltryptamine (5-MeO-NiPT).

Methods: Dose-response relationships (0.03 – 30 mg/kg s.c.) for the induction of head twitch responses and body temperature changes were determined in 30-min test sessions using male C57BL/6J mice. In separate experiments, the same endpoints were examined when mice were pretreated with either a 5-HT2A (M100907, 0.01 mg/kg s.c.) or 5-HT1A (WAY-100635, 3 mg/kg s.c.) antagonist, prior to agonist administration. Total head twitch responses and body temperature changes were subjected to nonlinear regression analyses to calculate ED50 potency and Emax values. Differences between treatment conditions in dose-response (n = 5 – 7/group) and antagonist (n = 4 – 6/group) studies were assessed using one-way ANOVA followed by Dunnett's or Tukey's post hoc test ($p < 0.05$).
Results: Rank order of potency for head twitch responses in dose-response experiments was 5-MeO-MiPT > 5-MeO-NiPT ≥ 5-MeO-DiPT. Emax values for total head twitches revealed that 5-MeO-MiPT and 5-MeO-DiPT had similar maximal efficacy (~50 - 60/ 30 min), which was ~2.5 - 3x greater than that of the metabolite 5-MeO-NiPT (~20/ 30 min). Rank order of potency for causing hypothermia was 5-MeO-MiPT ≥ 5-MeO-DiPT > 5-MeO-NiPT. All compounds produced maximal temperature reductions of ~6 °C and potency for head twitch responses was greater than potency for hypothermic effects. Head twitches were blocked by M100907 pretreatment whereas temperature effects were blocked by WAY100635 pretreatment.
Conclusions: 5-MeO-MiPT, 5-MeO-DiPT, and 5-MeO-NiPT display agonist psychedelic-like activity at 5-HT2A receptors. These same compounds produce hypothermia at higher doses via agonist actions at 5-HT1A receptors.
Financial Support: NIDA IRP support to MHB

CHEMOGENETIC INHIBITION OF ACCUMBENS MICROGLIA REDUCES NICOTINE SEEKING

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Microglia are activated following nicotine self-administration (SA), and this is a critical neuroimmunological response in the nicotine-induced cellular signaling cascade in the nucleus accumbens core (NAc). While changes in microglia and inflammatory function have been characterized following nicotine exposure, the role of microglia in nicotine seeking behavior has not. Further, it has been a challenge in the field to virally transduce microglial cells in vivo. Thus, the goals of the current study were to (1) validate a recombinase-driver transgenic methodology to chemogenetically control NAc microglial activation prior to nicotine-cue reinstatement, and (2) determine the role of NAc microglia in nicotine-seeking behavior.
Methods: The current experiments utilized a cre-recombinase-expressing rat line, the LE-Tg(Cx3cr1-cre)3Ottc strain, which we verified via co-localization of Iba1 immunohistochemistry and fluorescence from intra-NAc cre-dependent Designer Receptor Exclusively Activated by Designer Drugs (DREADD) constructs in microglia. This approach was utilized to inhibit or stimulate NAc microglia of male and female rats immediately prior to nicotine cue-induced reinstatement. Following nicotine SA (0.06 mg/kg/infusion, FR1, paired with a light+tone compound stimulus) and extinction training, intra-NAc clozapine-N-oxide was administered 15 minutes prior to reinstatement. Rats were then sacrificed for analysis of microglial activation and electrophysiological recording of glutamate plasticity.
Results: Preliminary findings show that chemogenetic inhibition of microglia reduces cue-induced nicotine seeking within 15 minutes (trend: ANOVA; $p=0.056$). Ongoing analyses are determining if chemogenetic inhibition of microglia results in morphological changes, as well as reductions in reinstatement-induced increases in NAc glutamate plasticity (measured via AMPA/NMDA ratio).
Conclusions: While our prior research shows a neuroinflammatory response to nicotine within the reward pathway, our current findings suggest a critical role of microglia in driving nicotine seeking behavior using a novel chemogenetic approach. Further research will determine alterations in specific neurobiological endpoints involved in the modulation of nicotine seeking by microglia.
Financial Support: Funding: National Institute on Drug Abuse grant R01DA046526, R21 DA049130, R21 DA044479, DA045881 (to CDG)

INTERMITTENT THETA BURST STIMULATION (ITBS) TO MODULATE ATTENTIONAL BIAS FOR CIGARETTES IN PEOPLE WITH OPIOID USE DISORDER (OUD)

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: People with OUD smoke at four times the rate of the general population. The efficacy of currently approved pharmacotherapeutics for smoking cessation is suboptimal in this population. Novel interventions are needed. Brain stimulation could be a viable option to augment smoking cessation strategies. iTBS reduced the urge to smoke in a pilot study and increased abstinence at three months compared to sham TBS. Cigarette-cue attentional bias (AB) is a robust predictor of cigarette relapse. There is little work determining the effects of TBS on predictors of relapse and brain connectivity in smokers with OUD. The present, ongoing study is examining the effects of four active iTBS sessions versus sham on cigarette-cue AB and functional connectivity in OUD patients who smoke. We hypothesize iTBS will decrease AB relative to sham and produce differences in functional connectivity.
Methods: Cigarette-using OUD participants, stabilized on medications for opioid use disorder (MOUD) were recruited and randomized to either four sessions of active iTBS (N=2; 1800 pulses delivered at 120% resting motor threshold) or sham TBS (N=2). A stress paradigm was administered to participants at baseline before iTBS or sham TBS. Stimulation was delivered over dorsolateral prefrontal cortex (DLPFC), using MNI co-ordinates. Cigarette-cue AB was measured using eye-tracking and resting state functional connectivity scans were obtained at baseline and after four sessions for all participants.
Results: iTBS decreased cigarette-cue AB compared to sham ($p = 0.06$ and 0.2, respectively). Four sessions of iTBS decreased functional connectivity within bilateral middle and inferior temporal gyri at modified thresholds, which was not seen with sham TBS.
Conclusions: These findings suggest iTBS could be a promising adjunct to current smoking cessation strategies in patients with OUD.
Financial Support: Internal funding from Substance Use Research Priority Area (SUPRA), University of Kentucky College of Medicine

CONSTITUTIVE EXPRESSION OF HIV-1 VIRAL PROTEINS DELAYS DEVELOPMENT OF MEDIUM SPINY NEURONS IN THE NUCLEUS ACCUMBENS

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Drug Category Other, Adolescent Substance Use; Comorbidities
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The growing population (approximately 2.78 million) of children and adolescents living with either perinatally or horizontally acquired human immunodeficiency virus type 1 (HIV-1) appear uniquely vulnerable to developing problematic substance use. Indeed, perinatally infected adolescents living with HIV-1 (pALHIV) exhibit a faster development of substance use symptoms relative to perinatally exposed, but HIV-uninfected, youth. However, the neural mechanism(s) underlying the unique vulnerability of pALHIV to substance use remain unclear. It was hypothesized that neurodevelopmental alterations would be observed in medium spiny neurons (MSNs) in the nucleus accumbens (NAc) of HIV-1 transgenic (Tg) rats.
Methods: A time-sequential longitudinal experimental design was utilized to evaluate MSNs in the NAc with sample sizes of n=40 at each age (Control: Male, n=10, Female, n=10; HIV-1 Tg: Male, n=10, Female, n=10). Fischer (F344/N) HIV-1 Tg and control rats were sacrificed every 30 days from postnatal day (PD) 30 to PD 180. A ballistic labeling technique and confocal microscopy were utilized to visualize MSNs. Neuronal and dendritic spine morphology were evaluated using sophisticated neuronal reconstruction software.

Results: Preliminary analyses revealed a delayed development of the dendritic arbor in HIV-1 Tg, relative to control, animals evidenced by differences in the best fit function (i.e., HIV-1 Tg: First-Order Polynomial, R2≥0.91; Control: Horizontal Line). Furthermore, HIV-1 Tg animals exhibited alterations in dendritic spine development, evidenced by measurements of key dendritic spine morphological parameters (Genotype*Age*Bin Interaction: Backbone Length [$F(80,3312)=13.7$, $p\leq0.001$], Head Diameter [$F(60,2484)=39.5$, $p\leq0.001$], and Neck Diameter [$F(60,2484)=26.3$, $p\leq0.001$]). Specifically, morphological parameters of dendritic spines in HIV-1 Tg rats support a more immature dendritic spine phenotype early in development relative to control animals; however, genotypic differences in dendritic spine morphology dissipate across time.
Conclusions: Delayed development of MSNs in the NAc may mechanistically underlie the unique vulnerability of pALHIV to addiction.
Financial Support: NIH Grants DA013137, HD043680, MH106392, NS100624

ORAL COMMUNICATION: CANNABINOID SCIENCE

BEHAVIORAL AND NEUROCOGNITIVE EFFECTS OF A MINOR CANNABINOID CANNABIGEROL (CBG)

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Cannabigerol (CBG) is a minor cannabinoid with growing popularity in retail cannabis products, and is touted as having therapeutic benefits for appetite stimulation, analgesia, and mood. This study characterized the pharmacological effects of CBG in a battery of tasks to assess appetitive behavior, motor impairment and neurobehavioral performance in rats.
Methods: Male and female Sprague-Dawley rats (N=48; 50% female) were assigned to the different test groups and orally administered CBG in sesame oil (30-600 mg/kg). Locomotor activity was assessed for 4-hours post-administration to determine stimulatory and/or sedative effects. Appetitive effects of CBG were determined in an operant task using a progressive ratio schedule of chow pellet reinforcement. Effects of CBG on attention were assessed with the rodent Psychomotor Vigilance Test (rPVT). Working memory was determined with the Y-maze spontaneous alternation task. ANOVAs or mixed models (sex and CBG dose as factors) were used to analyze distance traveled (activity), % spontaneous alternation, progressive ratio breakpoints, and rPVT outcomes of % accuracy, % lapses, % false alarms, and reaction times.
Results: CBG had modest stimulatory effects on locomotor activity in the first hour after administration. Sex specific effects of CBG were observed on attention (Sex x CBG Dose interaction; $p<0.001$); CBG impaired rPVT performance in females at high doses (300-600 mg/kg) but had no effect at any dose in males. In contrast, CBG (600 mg/kg) impaired working memory in the Y-maze, particularly in males (main effect of CBG; $p=0.02$). CBG did not affect appetitive behavior.
Conclusions: CBG had modest, but appreciable stimulatory effects on motor activity and impaired neurocognitive behavior. Interestingly, effects on attention were sex-dependent, and limited to female rats. Additional studies are ongoing to assess effects of CBG in combination with THC.
Financial Support: Supported by the Johns Hopkins University Dalio Fund in Decision Making and the Neuroscience of Motivated Behaviors. CBG was provided by Canopy Growth Corporation as a gift.

ADVERSE RESPIRATORY SYMPTOMS WITH CANNABIS VAPING WITH ENDS

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research

Aim: We examined the longitudinal associations between adverse respiratory symptoms among U.S. adolescents who initiated use of cigarettes, e-cigarettes, and cannabis with electronic nicotine delivery systems (ENDS) within a 12-month period.
Methods: We used Waves 4 and 5 data (N=8046) from the 12- to16-year-old sample of the Population Assessment of Tobacco and Health (PATH) Study. Retention was 88.4%. Multiple logistic regression assessed whether initiation of cigarette, e-cigarette, or cannabis vaping with ENDS was associated with past-year adverse respiratory symptoms.
Results: Lifetime vaping cannabis with ENDS was 4.9% (Wave 4) and 17.1% (Wave 5). Five respiratory symptoms were examined, with only two reaching significance. The odds of "wheezing or whistling" in the chest at Wave 5 were roughly thirty percent higher (aOR 1.32; 95% CI 1.05-1.68) among those who initiated cannabis vaping between Waves 4 and 5 with ENDS compared to those who did not. Neither the initiation of e-cigarettes nor cigarettes had a significant association with past-year “wheezing or whistling” in the chest. Models adjusted for history of cigarette and e-cigarette use, “wheezing or whistling” in the chest during Wave 4 and diagnosis of asthma. Fully adjusted models also found that the odds of indicating a past-year “dry cough at night that is not associated with a cold/chest infection” at Wave 5 were roughly thirty percent higher (aOR 1.28; 95% CI 1.04-1.56) among those who had initiated cannabis in ENDS compared to those who did not. Neither the initiation of e-cigarettes nor cigarettes at Wave 5 had a significant association with adverse respiratory symptoms in the fully adjusted models.
Conclusions: This study provides longitudinal evidence that adolescents' cannabis vaping with ENDS may have negative health consequences. Initiation of cannabis use with ENDS was substantially associated with higher odds of respiratory symptoms.
Financial Support: This research was supported by the National Institute on Drug Abuse (R01DA043696 and R21DA051388), National Cancer Institute (R01CA212517), and National Institute on Alcohol Abuse and Alcoholism (R01AA025684), National Institutes of Health.

EVALUATION OF CYTOCHROME P450-MEDIATED CANNABINOID-DRUG INTERACTIONS IN HEALTHY ADULT PARTICIPANTS

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Drug Category Cannabis/Cannabinoids
Topic Drug Interactions
Abstract Detail Human
Abstract Category Original Research
Aim: Evaluate the impact of cannabis extracts containing delta-9-tetrahydrocannabinol (THC) or THC and cannabidiol (CBD) on the pharmacokinetics (PK) of 5 target cytochrome P450 (CYP) enzymes and relation between the THC-CBD interaction and THC pharmacodynamics (PD).
Methods: Healthy adult participants (n=11) completed three, randomized, drug administration sessions. Each participant consumed a brownie containing a cannabis extract with 20mg THC, 20mg THC + 640mg CBD, or no cannabis extract (placebo), followed 30 min later by an oral CYP probe drug cocktail: caffeine 100mg (CYP1A2), losartan 25mg (CYP2C9), omeprazole 20mg (CYP2C19), dextromethorphan 30mg (CYP2D6), and midazolam 2mg (CYP3A). PK of these probes act as reporters of targeted CYP enzyme activity *in vivo*. Plasma samples were collected, and PD measures (vital signs, subjective drug effects, cognitive task performance) were obtained 0-24 hours after cocktail administration. PD outcomes were analyzed using 2-way ANOVA with condition and time as repeated measures (n=11). Plasma samples from the first 6 participants were analyzed using noncompartmental PK analysis to estimate area under the curve ($AUC_{0\text{-}t}$); the geometric mean ratio of $AUC_{0\text{-}t}$ was computed relative to the placebo or THC condition.
Results: CBD+THC increased THC $AUC_{0\text{-}t}$ and 11-OH-THC/THC $AUC_{0\text{-}t}$ ratio by 2.3- and 3.9-fold, respectively, due to inhibition of CYP2C9-mediated THC metabolism to 11-OH-THC and UGT-mediated 11-OH-THC metabolism. CBD inhibition of THC metabolism increased the magnitude and time course of heart rate, subjective effects, adverse events, and cognitive impairment. CBD+THC, but not THC, inhibited CYP1A2, 2C9, 2C19, and 3A activities as the $AUC_{0\text{-}t}$ of caffeine, losartan, omeprazole, and midazolam increased by 1.4-, 1.7-, 3-, and 1.7-fold, respectively. Cannabis extracts did not alter CYP2D6 activity.

Conclusions: Cannabis extracts containing THC+CBD produced PK drug interactions and stronger PD outcomes than THC. Dose adjustment should be considered for pharmaceutical drugs co-consumed with cannabis products depending on the THC:CBD ratio and dose used.
Financial Support: NIH grants U54 AT008909 and T32 DA007209

GENDER BY AGE DIFFERENCES IN TRAJECTORIES OF CANNABIS, ALCOHOL, AND TOBACCO CO-USE AMONG CANNABIS-USING YOUNG ADULTS DURING PRE- AND POST-RECREATIONAL CANNABIS LEGALIZATION (RCL) IN LOS ANGELES

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Rates of co-use of cannabis with alcohol and tobacco is rising among young adults which have significant prevention and intervention implications. Investigations examining changes in cannabis co-use with alcohol and tobacco pre- and post-recreational cannabis legalization (RCL) among young adult users are lacking. This study examines differences in parallel growth trajectories of cannabis, alcohol, and tobacco use among four user groups based on gender identity and age.
Methods: 366 cannabis-using young adults (aged 18-26) comprising 210 medical cannabis patients and 156 non-patients were surveyed annually from 2014-2020 in Los Angeles. Parallel process spline growth models examined co-occurring growth trajectories of cannabis, combustible cigarette, e-cigarette, and alcohol use over six years, with three waves pre-RCL and three waves post-RCL. Multi-group analyses examined differences in parallel processes between four ageXgender subgroups: a) younger (aged 18-21 at baseline) and b) older (aged 22-26) females; and c) younger and d) older males after accounting for differences based on race/ethnicity, cannabis patient status, and medicinal/recreational use.
Results: All substance use exhibited a general decline over time except for e-cigarettes. When examined based on subgroups, post-RCL, older females were the only group with an increase in cannabis use. Cannabis had significant relationships with other substance use depending on subgroup. In younger females, there was a simultaneous increase in cannabis and combustible cigarette usage in both pre- and post-RCL. Older females saw a negative relationship between cannabis and e-cigarette usage post-RCL. Initial level of cannabis use was associated with decreased alcohol use pre-RCL and increased use in post-RCL for younger males. Patient status at baseline predicted greater initial levels of cannabis use across all subgroups. Racial/ethnic group differences were also observed.
Conclusions: This study provides novel findings on cannabis and other substance co-use trajectories based on age and gender, and other characteristics which can inform current knowledge and targeted interventions.
Financial Support: NIDA grant DA034067

ORAL COMMUNICATION: THE ROLE OF NEIGHBORHOOD ON SUDS

RACIAL DIFFERENCES IN THE RELATIONSHIP BETWEEN NEIGHBORHOOD SOCIAL CAPITAL AND OPIOID MISUSE AMONG JUSTICE-INVOLVED ADOLESCENTS

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Drug Category Opiates/Opioids
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid misuse (OM), mass incarceration, and systemic racism are three major interrelated social issues impacting adolescent health in the United States. Relative to adolescents in the general population,

justice-involved adolescents (JIA) are more likely to misuse opioids, stem from disadvantaged neighborhoods, identify as Black or Latinx, and suffer harsher consequences from OM. Disparities in risk for OM may be attributed to racial differences in the benefits of neighborhood social capital, a manifestation of systemic racism. However, these relationships have not been investigated. This study tests the hypothesis that social capital reduces the risk for OM, but these benefits are diminished for Black and Latinx JIA relative to White JIA.
Methods: Stratified logistic regression was employed to analyze a statewide sample of 79,570 JIA from the Florida Department of Juvenile Justice (FLDJJ). This sample represents all youth who (a) received one or more arrests for delinquency, (b) completed the full intake assessment, and (c) reached the age of 18 by the year 2016. Past 30-day OM was derived from urine analysis and self-reported data. Neighborhood social capital was operationalized by census response rates and the Child Opportunity Index.
Results: Results indicate that neighborhood social capital was associated with a 50% decrease in the odds of OM among White and Latinx JIA, but only a 10% decrease in odds among Black JIA.
Conclusions: Systemic racism may reduce the capacity for certain racial groups to access and capitalize on neighborhood social capital. Stakeholders can implement diversity, equity, and inclusion plans to ensure that investments in institutions to resolve the opioid crisis equitably benefit diverse racial groups.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

FAMILY, NEIGHBORHOOD AND INDIVIDUAL FACTORS LINKED TO EARLY SIPPING AS IDENTIFIED BY MACHINE LEARNING ANALYSIS

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Drug Category Alcohol
Topic Artificial Intelligence
Abstract Detail Human
Abstract Category Original Research
Aim: Children's sipping of alcohol is associated with later alcohol and substance misuse. Here, we used machine learning methods to identify predictors of early sipping across three domains, namely, 1) environmental, 2) psychological, and 3) health factors. We hypothesized that environmental factors would be most predictive of early alcohol sipping during childhood.
Methods: Using the Adolescent Brain and Cognitive Development (ABCD) study sample (N=10,707; N=1498 sippers, 42% female), we classified sipping by age 10 with eXtreme Gradient Boosting (XGBoost), excluding those that drank accidentally, furtively, or for religious reasons. Nested cross validation evaluated the area under the receiver operating characteristic curve (AUC) for each model. We then employed SHapley Additive exPlanations (SHAP) to rank the unique contribution of the included predictors per model (environmental: 341, psychological: 127, health: 359).
Results: As hypothesized, the environmental (AUC=0.755) outperformed the health (AUC=0.676) and psychological (AUC=0.653) models. Top-ranked environmental predictors linked to early sipping included easy access to alcohol, high weekend screen time, low parental religiosity, high parental alcohol use, high socioeconomic status and low parental responsiveness to the child's negative affect. Health factors related to sipping included indicators of early pubertal onset, prolonged sleep, and mental health indicators. Low-level prodromal psychosis symptoms, and especially self-harm, were highly impactful. Lastly, the psychological model indicated that high sensation seeking, negative urgency, impulsivity and low school competency were predictive of early sipping.
Conclusions: As hypothesized, family-related factors were most predictive of early onset of alcohol use during childhood. However, psychological factors such as impulsivity and sensation seeking, also predicted early first alcohol use. Importantly, our results also indicate an important role of physical development and mental health factors. We anticipate that as the ABCD study children grow older, these individual factors will play an increasingly important role for predicting emergence of patterns of substance misuse.
Financial Support: AM is funded by the National Institute of Neurological Disorders and Stroke (T32NS105604-04; PI: Redish)

PARTNER INCARCERATION AND MATERNAL SUBSTANCE USE: INVESTIGATING THE MEDIATING EFFECTS OF SOCIAL SUPPORT AND NEIGHBORHOOD COHESION

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Drug Category Other, Substance use
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The United States is responsible for the highest rate of incarceration globally. This study aimed to investigate the impact of partner incarceration on maternal substance use and conduct exploratory mediation by financial support, emergency social support, and neighborhood cohesion.
Methods: Using data from the Fragile Families and Child Wellbeing Study, a longitudinal cohort following new parents and children, we examined the relationship between paternal incarceration and maternal substance use (N=2246). Responses from mothers at years 3 (2001-2003), 5 (2003-2006), 9 (2007-2010), and 15 (2014-2017) were assessed, restricted to mothers who responded across waves. Exploratory mediation by neighborhood cohesion, financial support, and emergency social support was investigated. Confirmatory factor analysis was employed to construct support-related mediators. Items were weighted by factor loadings and responses were summed to create a scale for financial support and emergency social support. Impact of partner incarceration and maternal substance use was modeled using multilevel modeling to account for repeated measures, adjusting for appropriate confounders (age of mother at child's birth, race, education, employment, and history of intimate partner violence).
Results: Nearly half (42.7%, N=958) of participants reported partner incarceration. Among mothers who described partner incarceration, the odds of reporting substance use are 96% (adjusted Odds Ratio [aOR]: 1.96; 95% Confidence Interval (CI):1.56-2.46) greater in comparison to those who reported no partner incarceration. Financial support at year 5 was a partial mediator of partner incarceration and substance use at year 9 (p-value = 0.006); financial support at year 9 was not a significant mediator. Neither emergency social support nor neighborhood cohesion were significant mediators at either year 5 or year 9.
Conclusions: Findings demonstrate that partner incarceration impacts maternal substance use. Financial support acts as a partial mediator in the short term, which has important social support implications for families disrupted by mass incarceration.
Financial Support: T32DA031099 (PI: Hasin).

EXAMINING HIV-MEDICATION ADHERENCE BY IMPULSIVITY AND NEIGHBORHOOD CHARACTERISTICS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: Adherence to HIV medications is necessary for viral suppression, but can be difficult to achieve consistently. Lower adherence has been associated with (1) personal factors, such as impulsivity and sensation seeking, and (2) adverse environmental factors. We explored whether adherence to HIV medications is related to interactions between neighborhood context and impulsivity or sensation seeking.
Methods: 243 HIV+ participants were drawn from a sample of 300 people (mean±SD age = 55±10 years, 61% male, 84% Black/African American) recruited to a cross-sectional study in Baltimore, Maryland. 74 HIV+ people reported past-month medication non-adherence (medication taken <100% of days). Neighborhood context was assessed with the Perceived Neighborhood Scale (PNS) and psychosocial hazards scores (derived from Baltimore Neighborhood Indicator Alliance data) incorporating social disorganization, public safety, physical disorder, and economic deprivation. Impulsivity was assessed with the Barratt Impulsiveness Scale (BIS). Sensation seeking was assessed with the Arnett Inventory of

Sensation Seeking (AISS). Differences in adherence (100% vs. <100%) were assessed by logistic regression.
Results: Participants were slightly more likely to have non-adherence if they had higher self-control impulsivity (BIS first-order factor): univariate, OR [95% CI] = 1.085 [1.002,1.180]; controlling for participant demographics, OR [95% CI] = 1.087 [1.000,1.184]. No other associations between BIS first- or second-order factors or AISS subscales and adherence were significant (0.978 [0.917,1.042] < OR [95% CI] < 1.065 [0.956,1.191]). For both the PNS subscales and psychosocial hazard scores, neighborhood context was not significantly related to adherence, either as a main effect or interaction with the BIS factors or AISS subscales (0.239 [0.0434,1.204] < OR [95% CI] < 3.002 [0.663,14.806]).
Conclusions: Overall, in our sample neither home neighborhood characteristics nor impulsivity and sensation seeking were strongly associated with HIV-medication adherence. Possible associations between self-control and medication adherence may merit further study, for example by additional assessment of executive function.
Financial Support: NIDA IRP

ORAL COMMUNICATION: THE NEUROSCIENCE OF ALCOHOL

BRAIN MORPHOLOGY PREDICTORS OF ALCOHOL, TOBACCO, AND CANNABIS USE IN ADOLESCENCE: A SYSTEMATIC REVIEW

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Drug Category Other, Substance use (Alcohol, Tobacco or Cannabis use)
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: In the last decade, extensive research has emerged on the predictive value of brain morphology for substance use initiation and related problems during adolescence. This systematic review provides an overview of longitudinal studies on potential pre-existing brain morphology variations and later initiation of alcohol, tobacco, and cannabis use.
Methods: Relevant literature from Embase, Medline ALL, Web of Science Core Collection, PsycINFO, Cochrane Central Register of Controlled Trials and Google Scholar was systematically searched to identify prospective longitudinal studies in which participants were substance-naïve at the structural neuroimaging measurement (N = 18). As this review focuses on the general population, participants were not specifically recruited as a member of a high-risk group e.g., those who were prenatally exposed to substances or had a family history of SUD.
Results: The current findings suggest that a smaller anterior cingulate cortex (ACC) volume, thicker or smaller superior frontal gyrus, and larger nucleus accumbens (NAcc) volume are associated with future alcohol use. Also, both smaller and larger volumes of the orbitofrontal cortex (OFC) were associated with future cannabis use and combined alcohol/cannabis use. Smaller amygdala volumes were related to future daily tobacco smoking.
Conclusions: These findings could point to specific vulnerabilities for adolescent substance use, as these brain areas are involved in cognitive control (i.e., the ACC), reward (i.e., the NAcc), motivation (i.e., the OFC), and emotional memory (i.e., the amygdala). The reported findings were inconsistent in directionality and laterality, and the largest study reported null findings. Therefore, future longitudinal large population-based cohort studies should investigate the robustness and mechanisms of these associations. We suggested future research directions regarding sample selection, timing of baseline and follow-up measurements, and a harmonization approach of study methods.
Financial Support: For my PhD project: Stichting Volksbond Rotterdam.

SEX DIFFERENCES IN RESPONSE INHIBITION NEURAL ACTIVATION IN BINGE DRINKING YOUNG ADULTS

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Drug Category Alcohol

Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Binge drinking is an early predictor of alcohol use disorders, and evidence suggests males are more vulnerable to binge drinking due to inhibitory control differences. Most neuroimaging studies examining sex differences in inhibitory control have utilized healthy participants; studies using at-risk or alcohol-using participants are limited. Here we investigate sex differences in inhibitory control in binge drinking young adults using a response inhibition task during fMRI.
Methods: Participants were 69 college students (M 19.4 ±0.8 years; 37 F) who screened positive for binge drinking via the AUDIT-C. Self-report estimates of daily drinking (past 30 days) and impulsivity (BIS-11) were collected. Response inhibition was assessed during fMRI using the go/no-go task (Correct Reject vs. Go). A one-sample t-test was run using all participants; mean activation from regions of interest (ROIs) meeting significance (FWE-corrected p=.05) were extracted and imported into SPSS. Individual t-tests were then run on each ROI to look for sex differences. In-scanner behavior was also collected (hit and false alarm rate, reaction times).
Results: Males had higher AUDIT-C scores (p=.01) and greater past 30- day drinking compared to females (p=.003). There were no sex differences for BIS-11 scores (p=.09). fMRI analyses revealed significant activation in six ROIs; of these three showed significant sex differences (males > females): right supramarginal gyrus (p=.03), right precentral gyrus (p=.01), and right insula (p=.06). Females did not show significantly greater activation than males in any of the ROIs. No sex differences were found for in-scanner behavior.
Conclusions: As expected, males reported more binge and daily drinking than females. Males had greater activation in three ROIs commonly reported as being part of the inhibitory control network. Since no sex differences for in-scanner behavior were found, one possibility is that males who binge-drink require more neural resources to successfully inhibit a prepotent response than females.
Financial Support: K01AA024804 (Hardee); K01DA044270 (Cope)

THE IMPACT OF AGE ON OLFACTORY ALCOHOL CUE-REACTIVITY: A FMRI STUDY IN ADOLESCENT VERSUS ADULT DRINKERS

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Drug Category Alcohol
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Previous work stresses the potential negative impact of alcohol use on the developing brain and the generally worse prognosis for early-onset Alcohol Use Disorders (AUDs). However, the high recovery rates of adolescent-onset AUDs suggest possible resilience. Little is known about the differential vulnerability of adolescents versus adults. This study aimed to investigate this by studying the relation between neural alcohol cue-reactivity, an important AUD biomarker, and the severity of alcohol use in adolescent compared to adult drinkers.
Methods: Brain activity in response to beer versus juice and water odors was recorded in low to high drinking adolescent (n = 50, 16-18 years) and adult (n = 51, 29-35 years) males matched on drinking severity. Beer and juice cravings were assessed before and after the task. Associations between beer odor cue-reactivity and AUD diagnosis, recent alcohol use, binge drinking, and craving were investigated across and between age groups in regions of interest (ROI) central in alcohol cue-reactivity; medial prefrontal cortex, anterior cingulate cortex, and striatal subregions. ROI analyses were complemented by exploratory whole-brain analyses.
Results: Pre-task beer cravings were negative but increased pre-to-post task in adolescents only. Individual differences in recent alcohol use, binge drinking, and craving did not relate to beer odor-induced activity. However, ROI and whole-brain analysis showed that within adolescents specifically, those that met DSM-5 criteria for AUD showed higher beer odor-induced activity in a large mesocorticolimbic cluster of voxels

encompassing the right caudate, nucleus accumbens, orbitofrontal cortex, and olfactory sulcus. This effect was absent in adults.
Conclusions: These findings point to adolescent risk rather than resilience and suggest a differential role of cue-reactivity in adolescent versus adult AUD. Furthermore, these findings highlight the urgency for studies investigating similarities and differences in the processes underlying the trajectories and treatment of adolescent versus adult AUD.
Financial Support: Brain and Cognition Project grant 2017 and ERC starting grant 2020 (no. 947761)

QUANTITY OF ALCOHOL CONSUMED ASSOCIATED WITH CHANGES TO 106 BRAIN MEASURES IN THE UK BIOBANK

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Drug Category Alcohol
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: The UK Biobank offers an unprecedented resource to study associations between self-reported alcohol use and changes in 945 imaging derived phenotypes (IDPs). We include IDPs representing global and regional structures from T1 MRI, lesions derived from T2 MRI, and white matter connectivity from dMRI. By referencing responses in the online mental health questionnaire (MHQ) we are able to precisely identify participants who engage in binge drinking. Our hypotheses are: 1) certain brain regions are more susceptible to increased alcohol consumption and 2) certain regions are particularly vulnerable to binge drinking behavior as opposed to lower level alcohol consumption.
Methods: Alcohol surveys and collection and processing of the MRI data to create the IDPs was done using standardized procedures. This study represents a subset of 25206 human subjects from the UK Biobank who had neuroimaging data and valid responses on the MHQ. We performed linear regression in R to determine the association between IDPs and alcohol use, controlling for both imaging and non-imaging related confounds. We compared models with and without a term for binge drinking.
Results: 106 IDPs showed a statistically significant association with alcohol measured as drinks per week ($p < 5.29x10-5$ to correct for multiple comparisons). These include a decrease in the volume of global grey matter an increase in ventricular CSF volume. There were changes to structure and connectivity in numerous regions including the frontal lobe and basal ganglia. Binge drinking did not achieve statistical significance for any IDPs suggesting there is no additional effect of binging over increased total consumption. The large sample size assures substantial statistical power to detect this effect if present.
Conclusions: The quantity of alcohol consumed has significant associations with adverse changes in multiple brain regions. Binge drinking behavior does not have any association outside of increased overall consumption.
Financial Support: Collaborative Study on the Genetics of Alcoholism (COGA) U10 AA008401, Multi 'Omics Integration and Neurobiological Signatures of Alcohol Use Disorder (AUD) R01 AA027049, Integrating Epigenomics in Human Brain and Genomics of Nicotine Dependence R01 DA042090, the UK Biobank Resource under Application Number 48123.

TUESDAY, JUNE 14, 2022

ORAL COMMUNICATION: BEHAVIORAL PHARMACOLOGICAL RESEARCH

AGOMELATINE, A CLINICALLY-AVAILABLE MELATONIN AGONIST, ATTENUATES ACQUISITION OF OPIOID-REINFORCED BEHAVIOR

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study

Abstract Category Original Research
Aim: Melatonin is known for its anti-addictive properties, which include attenuation of morphine-induced conditioned-place preference and precipitated withdrawal. Therefore, we determined whether the melatonin agonist agomelatine can decrease opioid-reinforced behavior. Agomelatine also acts as a serotonin 2C Antagonist.
Methods: After pretreatment with noncontingent morphine, male Wistar rats were test trained to self-administer morphine under a progressive-ratio schedule. Effects of agomelatine(3.2 or 10 mg/kg-day) was tested in acquisition, reinstatement, and reacquisition of morphine-reinforced behavior. We also evaluate its effects on naloxone-precipitated withdrawal.
Results: After chronic treatment with 3.2 or 10 mg/kg-day, acquisition of morphine-reinforced behavior was decreased by 36.4 and 60.6 %, respectively. Reductions were seen for animals responding under a progressive-ratio but not fixed-ratio schedules. In morphine-experienced rats, neither reinstatement nor reacquisition of morphine self-administration was altered. Agomelatine treatment also did not modify naloxone-precipitated withdrawal.
Conclusions: In opioid-naïve animals, chronic agomelatine pretreatment caused a dose-related decrease in levels of morphine self-administration. After rats acquired a stable level of self-administration, it was ineffective in modifying drug-reinforced behavior. It also failed to modify reinstatement or precipitated withdrawal. Taken together, these results suggest a role for melatonin agonists and related compounds in preventing rather than treating opioid use disorders.
Financial Support: Supported by grants I01 BX004748-01 (Department of Veterans Affairs) and 1R21DA037556-01 (NIDA) issued to KG

THE DUAL OPIOID RECEPTOR ANTAGONIST, SUVOREXANT, SELECTIVELY REDUCES STRESS-INDUCED REINSTATEMENT OF OXYCODONE-SEEKING BEHAVIOR BUT NOT SWEETENED CONDENSED MILK-SEEKING BEHAVIOR IN MALE RATS

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Opioid abuse and overdose have risen to epidemic proportions in the United States. Prescription opioids, such as oxycodone, are potent analgesics used to treat and manage pain. Oxycodone is one of the most commonly abused prescription drugs. The orexin (Orx) system is recruited by drugs of abuse, and it has been demonstrated that blockade of Orx receptors (OrxR) can prevent oxycodone, cocaine, and alcohol-seeking behavior. Because Orx transmission in the posterior paraventricular nucleus of the thalamus (pPVT) is pivotal in mediating drug-seeking behavior, the present study tested whether intra-pPVT administration of the FDA-approved dual orexin receptor antagonist, suvorexant (Sx), could prevent foot shock stress-induced reinstatement of oxycodone-seeking behavior.
Methods: 17 Male Wistar rats were trained to self-administer oxycodone (0.15 mg/kg/infusion, i.v.) by voluntary lever pressing, 8 h/day for 21 days (FR1, TO20). A separate group of rats was trained to self-administer a highly palatable food reward (sweetened condensed milk, [SCM], dilution 2:1 v/v, p.o., FR1, TO20). After training, rats underwent 2-h daily extinction training, during which oxycodone and SCM were withheld. Following extinction, the influence of intra-pPVT Sx (15 µg/0.5 µl) on stress-induced oxycodone and SCM-seeking behavior was tested and assessed with regression methods
Results: Rats progressively escalated oxycodone self-administration ($F(1,19)= 4.961$, $p \leq 0.0382$) with training and manifested significant physical signs of opioid withdrawal. Foot shock stress significantly reinstated oxycodone-seeking behavior, and intra-pPVT administration of Sx blocked this effect ($F(1,4)= 7.765$, $p \leq 0.0495$). For SCM, rats readily acquired self-administration ($F(1,19)= 44.40$, $p \leq 0.001$), and stress significantly reinstated SCM-seeking behavior, but intra-pPVT Sx did not modify stress-induced reinstatement of SCM-seeking behavior ($p > 0.05$).
Conclusions: The present findings suggest that OrxR signaling within the pPVT contributes selectively to stress-induced reinstatement of oxycodone-seeking behavior and may provide a promising target for future therapeutics to prevent stress-induced craving and relapse to prescription opioids.

Financial Support: This work was supported by The National Institute on Alcohol Abuse and Alcoholism (grant no. AA006420, AA026999, AA028549, and T32 AA007456).

FULL AND PARTIAL MGLU5 NEGATIVE ALLOSTERIC MODULATORS ATTENUATE COCAINE-RELATED BEHAVIORS AND INCREASE ACCUMBAL DOPAMINE CONCENTRATIONS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Negative allosteric modulators (NAMs) targeting the metabotropic glutamate receptor subtype 5 (mGlu5) may be a promising pharmacotherapy for cocaine use disorder (CUD). However, adverse effect risk of full mGlu5 NAMs has prompted the recent development of partial mGlu5 NAMs, a novel approach to maintain therapeutic effects while reducing adverse effect risk. Here, we compare the partial mGlu5 NAM M-5MPEP with full NAM VU0424238 on cue- and cocaine-induced reinstatement. Further, we examine the neurochemical effects of these compounds by measuring extracellular dopamine concentrations using in vivo microdialysis.
Methods: Male (n=55) and female (n=27) Sprague Dawley rats were trained to SA 0.5 mg/kg/infusion of cocaine. A vanilla odor cue was present in each session along with a light cue following each infusion. Responding was then extinguished with both cocaine and cues absent. Cues were then reintroduced in a single cue-induced reinstatement session. A cocaine-induced reinstatement session (10 mg/kg, i.p.) occurred 3 days later. M-5MPEP (18-56.6 mg/kg; i.p.) or VU0424238 (3-30 mg/kg; i.p.) were administered 30 min prior to each reinstatement session.
For in vivo microdialysis, probes were implanted into the nucleus accumbens (NAc) shell of male Sprague Dawley rats (n= 32). Dialysate samples were collected every 20 minutes for 4.5 hours with vehicle, VU0424238 (30 mg/kg), or M-5MPEP (56.6 mg/kg, i.p.) administered 2 hours into sampling and 30 minutes prior to a vehicle or cocaine (10 mg/kg, i.p.) injection. Dopamine concentrations were then quantified using high performance liquid chromatography (HPLC).
Results: M-5MPEP and VU0424238 attenuated cue-induced reinstatement. Only VU0424238 attenuated cocaine-induced reinstatement. Further, early results suggest both compounds reduce cocaine-induced increases in dopamine concentrations in the NAc shell.
Conclusions: Both full and partial mGlu5 NAMs sufficiently reduce cocaine-related behaviors. Dopamine changes provide a neurochemical correlate for the observed behavioral effects and, together, results support the development of both full and partial mGlu5 NAMs for CUD.
Financial Support: DA042129 and DA041349

PROGRESSIVE AND FIXED RATIO SCHEDULES OF COCAINE DELIVERY IN RATS CONVEY THE SAME INFORMATION

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Progressive ratio (PR) schedules of cocaine delivery are used to determine the 'motivational' state of the animal and cocaine's 'reinforcing efficacy'. This widely held interpretation is supported mainly by the observation that the PR breakpoint (BP) is proportional to the unit dose of cocaine. In contrast, under Fixed Ratio (FR) schedules the rate of cocaine self-injections are inversely proportional to the unit dose. The compulsion zone theory of cocaine self-administration explains cocaine self-administration under an FR-1 schedule and was applied to determine if it could also explain the pattern of lever-pressing and cocaine injections under a PR schedule in rats.

Methods: Male Sprague-Dawley rats were trained to self-administer cocaine using an FR-1 schedule across a range of unit doses from 0.3 to 12 μmol/kg (i.v.). In the same rats, cocaine was self-administered using a PR schedule across a range of unit doses.
Results: The inter-injection intervals during the FR-1 schedule were regular and proportional to the unit dose, explained by the time for cocaine levels to fall to the satiety threshold. The time for responding to extinguish is explained by the time for cocaine to levels to decline through the compulsion zone. Typical for the self-administration under PR schedules, long post-injection pauses occurred when calculated cocaine levels were above the satiety threshold. Lever-presses were observed only when cocaine levels were within the compulsion zone, the same as during the FR-1 sessions.
Conclusions: The compulsion zone theory interprets BP as the maximal number of responses which rats can perform after an injection while cocaine levels remain within the compulsion zone. The maximal BP at cocaine unit doses higher than the width of the compulsion zone (~3 μmol/kg) was the same as the total number of extinction presses after FR-1 self-administration. These data suggest that PR and FR schedules convey the same information.
Financial Support: DP1DA031386

ORAL COMMUNICATION: HARM REDUCTION EFFORTS FOR SUDS

HARM REDUCTION STORIES: LEVERAGING GRAPHIC MEDICINE TO ENGAGE VETERANS IN SUBSTANCE USE SERVICES WITHIN THE VA

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[1]Boston Medical Center, [2]Veterans Affairs Boston Center for Healthcare Organization and Implementation Research
Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Harm Reduction
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Harm reduction strategies, including safe injection education and efforts to engage people who inject drugs (PWID) in care, are vital to decreasing the morbidity and mortality associated with injection drug use (IDU). Graphic medicine refers to the use of comics and visual storytelling to personalize and illustrate a medical topic by chronicling an individual's experience and has been used successfully in public health campaigns and patient care. We describe the collaborative development of an innovative graphic medicine storybook intended to educate patients on the infectious risks associated with IDU and potential risk mitigation strategies.
Methods (Optional): We recruited a focus group of six Veterans with lived experience with IDU using purposive sampling. Over the course of twelve sessions, the group reviewed draft content, including clinical vignettes and educational material discussing infection prevention techniques and available VA resources, and worked with a graphic designer to develop a storybook incorporating the Veterans' input. In conjunction with this work, we also engaged participants in discussions to define key characteristics of patient-centered conversations about substance use and harm reduction education in order to develop subsequent provider-facing educational materials.
The storybook will be pilot-tested to explore the extent to which it achieves the intended goals of improving knowledge about infectious risks and risk mitigation strategies associated with injection drug use and resources within the VA available to PWID. Pilot participants will complete pre- and post surveys evaluating their knowledge of infection prevention techniques and relevant VA resources and will provide feedback on the storybook.
Conclusions: Graphic medicine is ideally suited for a patient-centered curriculum about harm reduction strategies. Results from this project will inform the development of a more comprehensive bundle of harm reduction interventions that will be integrated into VA facilities nationally.
Financial Support: LH is supported by BU-CHART (NIDA T32 AI052074) and RAMS (NIDA R25DA033211). WBE and JH are supported by VA HSRD Innovations grant (INV 20-099, WBE and JH, Co-PI). WBE is supported by NHLBI 1K12HL138049-01.

A MULTI-PHASE PILOT STUDY TO EVALUATE A NOVEL NALOXONE NASAL SWAB

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Current prescription naloxone products, for the emergency treatment of opioid overdose, experience accessibility and affordability barriers1. The FDA has called for over-the-counter (OTC) naloxone in an effort to increase availablilty3. In response, a novel naloxone nasal swab was developed with absorption and onset of action at least equivalent to currently available products while focusing on accessibility and affordability.
Methods: A multi-phase, inpatient crossover study compared bioavailability and plasma concentration levels of an intranasal naloxone swab (4, 8, 12mg) at early time points post-delivery (<15 minutes) with IM naloxone injection (0.4 mg) and naloxone nasal spray (4 mg) in healthy subjects and assessed the safety and tolerability. One of the two pilot phase tested the 12mg in as one and two doses and 8mg as two doses. This phase utilized an updated administration technique (squeeze nostrils) to improve bioavailability and faster plasma concentrations of naloxone.
Results: All nasal swab doses showed superior absorption and higher plasma concentrations (potential earlier onset of action) to both IM injection and intransal spray, demonstrated by, pAUC at 2.5 min (31.18 pg*hr/mL, 44.19 pg*hr/mL, 50.67 pg*hr/mL versus 4.19 pg*hr/mL, 11.81 pg*hr/mL, respectively). The Tmax for all nasal swab doses was comparable (Tmax 0.26 hr, 0.29 hr, 0.22 hr for single 12mg, two 12mg and two 8mg doses) to a single 0.4mg/mL IM injection (Tmax 0.25 hr) and faster onset than a single 4mg intranasal spray (Tmax 0.45 hr). Adverse events were mild for all treatments and no SAEs were observed.
Conclusions: Nasal swab application of naloxone is effective, well tolerated and is comparable to or exceeds key pharmacologic indices of existing approved naloxone products. The pilot phase provided a target dose for the final pivotal bioequivalence study. Safe, effective medication delivery in an OTC nasal swab, can address accessibility and affordability barriers of current naloxone products.
Financial Support: Study sponsored by Pocket Naloxone Corp

IMPACT OF COVID-19 PANDEMIC ON NALOXONE DISTRIBUTION AND TRAINING IN MARYLAND

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To examine the impact of COVID on (a) naloxone (opioid overdose reversal drug) distribution, and (b) naloxone education and training among responder groups before and during the COVID pandemic in Maryland.
Methods: We used provisional programmatic naloxone data from the Center for Harm Reduction Services, which operates a state-level community naloxone program. Individuals who received naloxone education and training were classified into two responder groups: social responders (people who use drugs [PWUD], family of PWUD) and occupational responders (law enforcement and outreach workers). Interrupted time series models compared pre-COVID (April 2019-March 2020) trends to trends during COVID (April 2020-March 2021).
Results: Pre-COVID, the average monthly naloxone distribution was 9,997 doses (95% CI=6,009, 13,986; p<0.001). Although there was a decrease in naloxone distribution at the start of COVID (95% CI= -12,932, 6,180; p=0.47), trends after April 2020 have remained stable (95% CI= -811, 877; p= 0.94).
Overall, 81,433 people were trained at 3,347 naloxone events from April 2019 to March 2021. Pre-COVID, number of individuals receiving naloxone education and training was increasing among occupational responders (95% CI= 61,121; p<0.001) and social responders (95% CI= 135, 496; p=0.002). The COVID

pandemic was associated with significant reduction in naloxone education and training among occupational responders (95% CI= -1224, -383; p=0.001) but not among social responders (95% CI= -4,320, 693; p=0.15). However, after April 2020, changes in trends were not significant among occupational responders (95% CI= -5, 82; p=0.08) and social responders (95% CI= -126, 388; p=0.30).
Conclusions: This Maryland-specific study provides preliminary evidence of disruptions and negative impacts of COVID on community naloxone distribution, and responder education and training at a time when opioid overdoses are rising. These findings call for sharing observations from other states with programmatic data to improve better understanding of the situation and help inform a timely response.
Financial Support: This study is funded by the Overdose Data to Action (OD2A) project supported by Cooperative Agreement number 6NU17CE924961 from the Centers for Disease Control and Prevention (CDC).

ORAL COMMUNICATION: COCAINE PRECLINICAL SCIENCE

EXAMINING SLEEP DISTURBANCES DURING COCAINE SELF-ADMINISTRATION AND ABSTINENCE IN RATS

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Animal Study
Abstract Category Original Research
Aim: There are no FDA-approved treatments for cocaine use disorder. As studies suggest that sleep disturbances during abstinence increase craving and risk of relapse among a variety of substance use disorders, reducing sleep impairments during abstinence may be a novel and effective treatment approach for CUD. Given that most human sleep assessments are subjective in nature and are assessed in patients with SUD or during abstinence, underlying effects of chronic drug exposure on sleep, even in animal models of SUD is lacking.
Methods: In the present study, electroencephalography (EEG) was used to observe sleep in drug naïve Sprague-Dawley rats (9 male/5 female) and following cocaine self-administration and subsequent abstinence. Rats were first trained to self-administer sucrose pellets during the first 2 hours of the dark cycle. Next, half continued to self-administer sucrose pellets, while the other half self-administered cocaine (0.75 mg/kg/inf) for 21 days. Rats then underwent 10 days of extinction and cue-induced reinstatement on the 7th day of extinction. EEG was recorded following the last day of sucrose pellet self-administration and every 5 days of cocaine self-administration or abstinence and manually scored as wake, rapid eye movement (REM) sleep, or non-REM sleep. Sleep was examined using within-subject changes from a drug-free baseline as well as between-group (food vs cocaine) changes.
Results: Preliminary analysis showed an increase in NREM sleep, specifically in the dark phase. Duration of REM sleep was unchanged, although percent REM of total sleep time decreased. Changes in sleep increased across the 21 days of cocaine self-administration, and persisted during the first few days of abstinence. Importantly, these alterations were not present in rats self-administering sucrose.
Conclusions: These data are the first to demonstrate progressive changes in sleep associated with cocaine self-administration and reiterate the need to normalize sleep disturbances as treatment approach for CUD.
Financial Support: This project was funded by DA042129 and Center for Research on Substance Use and Addiction (CRSUA), WFSM

IMAGING STUDIES OF THE KAPPA OPIOID RECEPTOR IN SOCIALLY HOUSED FEMALE AND MALE MONKEY MODELS OF COCAINE USE DISORDER

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Drug Category Stimulants
Topic Imaging
Abstract Detail Animal Study

Abstract Category Original Research
Aim: Cocaine use disorder (CUD) persists as a worldwide public health problem for which there is no FDA-approved pharmacotherapy. Using socially housed monkeys, we showed that there was an inverse relationship between dopamine (DA) D2/D3 receptors (D2/D3R) and vulnerability to cocaine abuse in males (subordinates more vulnerable than dominants), but the opposite in females (dominants more vulnerable than subordinates). The present study extended this characterization to include positron emission tomography (PET) imaging of the kappa opioid receptor (KOR) system; KOR and its endogenous ligand, dynorphin, are implicated in the neurobiological regulation of aversive states, stress and substance abuse. The first aim was to investigate KOR system, combining PET imaging with [11C]EKAP and primate social behavior in cocaine-naïve male and female monkeys (N=8/sex) living in same-sex social groups of 4/pen. The second aim of this ongoing study is to investigate how those baseline KOR measures change following chronic cocaine self-administration and to assess the neural plasticity of KOR system following protracted abstinence.
Methods: The primary dependent variable was binding potential (BP), which is an in vivo measure of the ratio of receptor density to receptor affinity. We examined 15 regions of interest and the highest BPs in all cocaine-naïve monkeys were in the claustrum and insula cortex.
Results: Comparing sex and social rank, we found that the lowest BPs across all regions of interest were observed in dominant females (Dom F) and subordinate males (Sub M); these are the two most vulnerable phenotypes to cocaine reinforcement.
Conclusions: For most regions, the rank order of BPs was Dom F < Sub M < Dom M < Sub F. Preliminary data in males indicates that after 100 mg/kg cocaine intake, the baseline differences between dominant and subordinate monkeys are exacerbated.
Financial Support: Supported by R01 DA017763-15 and T31 DA041349-05

THE SINGLE COCAINE DOSE REINSTATEMENT OF LEVER-PRESSING BEHAVIOR IN RATS IS EXPLAINED BY THE SATIETY THRESHOLD THEORY

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The satiety threshold model of the cocaine self-administration paradigm states that lever-pressing behavior is induced when cocaine levels fall to or below the satiety threshold. Single, injections of cocaine are known to reinstate lever-pressing in rats trained to self-administer cocaine. We investigated whether this phenomenon can be explained by the satiety threshold model.
Methods: Male Sprague-Dawley rats (n = 5) were trained to self-administer cocaine i.v. on an FR-1 schedule of cocaine delivery. These rats were administered a single non-contingent dose of cocaine (2 – 12 μmol/kg, i.v.) in four daily sessions per week, and the time to lever-pressing, the number of presses and the duration of pressing were recorded. Following reinstatement, lever presses had no consequences.
Results: The latency from the start of an injection to the resumption of lever pressing increased with the cocaine dose and ranged from approximately 2 min at 2 μmol/kg to more than 15 min at 12 μmol/kg.
Conclusions: The increasing latency to lever-pressing is consistent with the increasingly higher cocaine levels at higher doses taking longer to fall to the satiety threshold, while the lower doses start out within the compulsion zone. The number and duration of lever presses may reflect the time that the cocaine levels are within the compulsion zone. The cocaine satiety threshold model can account for the dose-dependent delay in reinstatement of lever-pressing behavior and is useful for understanding cocaine-induced responding in a rat model of cocaine use disorder.
Financial Support: u01DA050330

PROTECTING AGAINST COCAINE SEEKING BY ENHANCING COCAINE'S INNATE AVERSIVE EFFECTS IN RATS: MECHANISMS INVOLVING SEROTONERGIC RECEPTORS IN THE ROSTROMEDIAL TEGMENTAL NUCLEUS (RMTG)

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Drug Category Stimulants
Topic Mechanisms of Action
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Cocaine is strongly rewarding, but like many drugs of abuse, also produces aversive effects that influence drug-seeking, but that are not well understood. We show that serotonin signaling at the RMTg drives innate aversive responses to cocaine, that this aversive signal is downregulated by RhoA and PTEN in a subset of "vulnerable" rats, and that reversing this downregulation restores innate aversion to cocaine and protects against drug-seeking.
Methods: We used a combination of anatomical, behavioral pharmacological, and slice electrophysiological approaches.
Results: We found that cocaine depolarizes neurons of the rostromedial tegmental nucleus (RMTg), a major input to dopamine neurons. This depolarization is aversive and mediated by serotonin 2C receptors, and its magnitude correlates with individual differences in rats' behavioral avoidance responses to cocaine. These individual differences are due to downregulation of 5HT2CR signaling in "low-avoider" (but not high-avoider) rats via RhoA and PTEN-mediated dephosphorylation of this receptor. Blocking RhoA or PTEN reverses this dephosphorylation enhances cocaine avoidance in low-avoiders, reducing acquisition of cocaine-seeking.
Conclusions: The RMTg constitutes a substrate mediating innate aversive responses to cocaine. These responses are mediated by serotonin 2C receptors, but signaling by this receptor appears lost in a subset of "low-avoider" rats, making them particularly vulnerable to acquiring cocaine-seeking behavior. Mechanisms reversing the loss of signaling are a possible therapeutic target for treating or preventing cocaine use disorder.
Financial Support: NIDA/NIH R01

ORAL COMMUNICATION: OPIOID USE IN JUSTICE-INVOLVED PERSONS

IMPACT OF JAIL-BASED METHADONE OR BUPRENORPHINE TREATMENT FOR OPIOID USE DISORDER ON OVERDOSE MORTALITY IMMEDIATELY AFTER RELEASE FROM NEW YORK CITY JAIL, 2011-2017

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid overdose is a leading cause of death during the immediate time after release from jail or prison. Although methadone or buprenorphine treatment for opioid use disorder (MOUD) can reduce overdose risk, most jails in the United States do not provide MOUD, and its impact in jail settings is limited. To address this gap, we tested the hypothesis that in-jail MOUD is associated with lower overdose mortality risk post-release.
Methods: We used matched administrative records from New York City and New York State for analysis. The cohort consisted of 15,803 adults with opioid user disorder who were released from New York City jails to the community between 2011 and 2017. They experienced 31,388 incarcerations, which included 17,119 treatment (in-jail MOUD) and 14,269 comparison events (out-of-treatment). We conducted multivariable time-to-event data analysis. Specifically, to account for confounding on association between time-varying, non-random in-jail MOUD and overdose mortality, we performed the Cox regression model with time-invariant (gender), time-varying covariates (age, mental illness, prior incarceration count, felony charge, short jail stay, emergency department visits for 3 months prior MOUD events), and a frailty factor.
Results: Overall incarceration- and person-level characteristics were similar between the two groups except for a higher percentage of felony charges in the comparison group. For 1 year after release, 111 overdose

deaths occurred, and crude death rates were 0.49 and 0.83 per 100 person-years for in-jail MOUD and comparison groups, respectively. In-jail MOUD was associated with lower overdose mortality risk for 1-year post-release (adjusted HR = 0.59, 95% CI = 0.39, 0.91). Restricting data to the first month after jail release, the impact of in-jail MOUD became stronger (adjusted HR = 0.23, 95% CI = 0.09, 0.57).
Conclusions: In-jail MOUD lowers overdose mortality rates post-release and should be implemented in the United States jail system.
Financial Support: NIDA grant# R01DA045042-01A1.

RACIAL DIFFERENCES IN THE CONSEQUENCES OF OPIOID MISUSE AMONG MINORS IN THE CRIMINAL JUSTICE SYSTEM

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid misuse can have serious consequences for justice-involved adolescents. Black and Latinx adolescents are overrepresented in the justice system due to systemic racism and multidimensional social problems. Their communities and families are subject to harsher consequences due to a lack of access to healthcare and discriminatory drug policies. Youth at the intersection of opioid addiction, incarceration, and racism are extremely vulnerable to adverse life outcomes. Despite the recent surge in opioid deaths among Black individuals, there is a deficit of research on racial differences in the consequences of opioid misuse, particularly among justice-involved adolescents.
Methods: A scoping review was conducted to explore racial differences in the consequences of opioid misuse. In addition, logistic regression was employed to analyze a statewide sample of 79,960 JIA from the Florida Department of Juvenile Justice (FLDJJ). This sample represents all youth who (a) received one or more arrests for delinquency, (b) completed the full intake assessment, and (c) reached the age of 18 by the year 2016. Past 30-day opioid misuse was derived from self-reported data. Economic, family, health, and social consequences are explored.
Results: Less than 3% of the sample met the criteria for opioid misuse. However, opioid misuse was associated with alarming outcomes, and many of these consequences were exacerbated for Black and Latinx adolescents. For example, compared to non-opioid users, opioid misuse was associated with 2.6 times higher odds of attempting suicide among White adolescents, 3.3 times higher odds among Black adolescents, and 4.4 higher odds among Latinx adolescents, respectively.
Conclusions: Opioid misuse can have especially devastating consequences for Black and Latinx adolescents in the system. These data demonstrate the urgent need for treatment programs in minority communities.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

A QUALITATIVE INVESTIGATION OF PERCEPTIONS OF COMMUNITY CORRECTIONS AND TREATMENT EXPERIENCE AMONG PEOPLE WITH INCARCERATION HISTORIES RECEIVING OUTPATIENT METHADONE TREATMENT

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human

Abstract Category Original Research
Aim: The experiences of criminal justice system involvement among individuals receiving methadone treatment (MT) for opioid use disorder (OUD) are poorly understood. We investigated perceptions of community correction and treatment experiences among individuals currently receiving MT in the community with a history of incarceration.
Methods: From January-December 2017, an experienced qualitative research team conducted individual, in-person, semi-structured interviews about incarceration and treatment experiences with patients receiving MT. Forty-two participants (19 female, 23 male) were each compensated $25 after completing the interview and demographics form. The interviews were audio-recorded, transcribed, and de-identified, and then independently coded by two members of the research team (a medical student and a clinical psychologist) using NVivo.
Results: Mean age was 42.9 years (SD=10.1, range 26-70); 23 (57%) identified as white, 10 (24%) as Black, and 8 (19%) as Hispanic. Participants' self-reported number of times incarcerated ranged from 1 to 60 (median 4.0, 25th IQR =2.0, 75th IQR = 8.3). Most participants described positive perceptions of and experiences with community corrections officers, yet most viewed the community corrections system negatively overall. Most participants perceived community corrections officers to have varying levels of knowledge of OUD treatment, and minimal knowledge about MT. Few participants noted assistance from community corrections with seeking MT or community-based addiction care.
Conclusions: Our findings suggest that while individuals with incarceration experience receiving MT have negative experiences with the community corrections system, they perceive individual community corrections officers positively. Understanding and knowledge of evidence-based treatment for OUD among community corrections officers may vary. Interventions that address and improve gaps in community corrections officer's knowledge of OUD and MT are needed to optimize support for individuals on probation or parole with OUD to improve entry and retention in OUD treatment.
Financial Support: DTB is supported by National Institutes of Health U01 HL150596-01 (DTB) and RM1 DA055310 (DTB). This work was also supported by the APT Foundation.

THE IMPACT OF THE COVID-19 PANDEMIC ON THE TREATMENT OF OPIOID USE DISORDER AMONG POPULATIONS WITH JUSTICE INVOLVEMENT: A CROSS-SECTIONAL STUDY

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: The COVID-19 pandemic disrupted health care delivery everywhere. Populations with justice involvement have a disproportionate burden of opioid use disorder (OUD) and vulnerability to infectious disease, necessitating rapid development of protocols to sustain care delivery while mitigating the risk of COVID-19 transmission. This study assessed OUD treatment changes among carceral and community treatment programs (CTP) participating in the Long-Acting Buprenorphine vs. Naltrexone Opioid Treatments in Criminal Justice System-Involved Adults (EXIT-CJS) study.
Methods: In September 2020, a cross-sectional web-based survey was sent to 6 carceral and 7 CTP sites participating in EXIT-CJS. The survey assessed changes in program census, OUD management, telehealthcare delivery, and re-entry support implemented after the onset of the COVID-19 pandemic (i.e., April-September 2020), compared to pre-pandemic (i.e., January-March 2020).
Results: All carceral sites (n=6) reported decreased overall monthly admissions. Similarly, most CTPs (n=4/7) reported decreased admissions for OUD, while 2 reported increased admissions for OUD. Less carceral (n=2/6) than CTP (n=6/7) sites reduced in-person medical visits. All carceral sites with pre-COVID telemedicine use (n=5/6) either increased or maintained telemedicine. All CTPs providing medication for opioid use disorder (MOUD; n=6/7) increased telemedicine use. Among carceral sites, half (n=3/6) increased MOUD inductions. Two increased MOUD maintenance and half (n=3/6) experienced no change

in MOUD maintenance. Most CTPs (n=4/7) reported no change in MOUD induction or maintenance. While most carceral and CTP sites maintained the capacity to provide MOUD, their capacity to provide community re-entry support declined.
Conclusions: Overall, this small sample of carceral and CTP sites operationally maintained or expanded MOUD delivery by utilizing telemedicine. However, potential capacity challenges (e.g., reduced re-entry supports, decreased OUD treatment admissions) may create new gaps in services provided to populations with justice involvement. Future research should explore strategies to sustain innovations in OUD treatment delivery while maintaining comprehensive intakes and re-entry supports during societal crises.
Financial Support: The EXIT-CJS study is funded by NIDA U01DA047982 (PIs: Lee, Farabee, Marsch, Gryczynski, Springer, Waddell).

ORAL COMMUNICATION: PRENATAL SCIENCE II

EFFECT OF IN-UTERO POLYSUBSTANCE EXPOSURE ON ADOLESCENT CARDIOVASCULAR DISEASE RISK: RESULTS FROM THE MATERNAL LIFESTYLE STUDY

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Polysubstance use during pregnancy typically includes use of one or more illicit substances in addition to tobacco and/or alcohol. Rates of polysubstance use during pregnancy range from 5-10% and continue to increase each year. However, to date there are no studies using longitudinal data exploring cardiovascular disease risk in adolescents exposed to polysubstances in utero. The aim of this analysis was to compare systolic blood pressure at age 16 among adolescents who were and were not exposed to singular and polysubstance use in utero.
Methods: The National Institute on Drug Abuse (NIDA)-funded Maternal Lifestyle Study (MLS) cohort was used for this analysis. Briefly, in 1993 MLS enrolled mothers (n=1,388) by substance use during pregnancy status (Y/N) at four US locations (Detroit, MI; Miami, FL; Providence, RI; and Memphis, TN) and followed offspring (male and female) until 2011. Generalized linear modeling assessed cardiovascular disease risk in offspring via systolic blood pressure (elevated: >120mmHg) at age 16 comparing those exposed and not exposed to substances in utero.
Results: The most prevalent singular substance used during pregnancy in this sample was alcohol (n=196, 17%), while the most common polysubstance used during pregnancy was a tri-combination of tobacco, alcohol, and cocaine (n=191, 16%). Those born normal birthweight (>2500g) and exposed to tobacco, alcohol, and opioids in utero had 22 mmHg higher systolic blood pressure at age 16 compared to those not exposed to any substances, after adjusting for covariates (β coefficient = 22.44, 95% CI: 10.53-34.35).
Conclusions: Singularly, tobacco, alcohol, and opioids are among the most used during pregnancy and when used in combination, pose great risk for cardiovascular disease in offspring. Given its recent rise and high prevalence, targeting maternal substance use is critical for cardiovascular disease prevention.

PRENATAL CANNABIS EXPOSURE MODERATES THE RELATIONSHIP BETWEEN SLEEP HOURS AND INTERNALIZING PROBLEMS: A CAUSAL INFERENCE ANALYSIS OF ABCD DATA

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Drug Category Cannabis/Cannabinoids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: A 2019 epidemiological survey reported that 5.4% of women used cannabis during their pregnancy, yet we do not understand if this exposure is causally related to child health. Prior studies suggest that prenatal cannabis exposure is associated with poor sleep and internalizing problems in children. Therefore,

using the potential outcomes framework and statistical causal inference methods applied to the Adolescent Brain and Cognitive Development (ABCD) study, it was hypothesized that prenatal cannabis exposure would moderate a causal relationship between sleep hours and internalizing problems.
Methods: A causal random forest model leveraged baseline (age 9-10) and 1-year follow-up ABCD data (N=9,826) to test if prenatal cannabis exposure (n=605) moderated the effect of a change in sleep hours on internalizing problems. Causal random forests flexibly model interaction terms from a set of covariates (prenatal cannabis, alcohol, and tobacco exposure, sociodemographics, etc.) to uncover moderation effects for a hypothesized causal pathway.
Results: On average, increasing sleep hours was related to decreasing internalizing problems (average treatment effect =-0.36, Std.Err.=.08). Moreover, this effect was moderated by prenatal cannabis exposure (heterogeneous treatment effect=0.13, Std.Err.=27), but not prenatal alcohol or cigarette exposure (or other covariates). Specifically, whereas more sleep was associated with less internalizing problems, this effect was absent in children exposed to cannabis in-utero.
Conclusions: While future studies will investigate why children with prenatal cannabis exposure exhibit divergent effects, these findings underscore using causal inference to uncover individual differences in child mental health outcomes. Similar approaches with future ABCD data will be undertaken to model adolescent cannabis initiation as an exposure or outcome measure.
Financial Support: The research conducted at the Laureate institute for Brain Research was supported by the William K. Warren Foundation. The ABCD Study is supported by the National Institutes of Health and additional federal partners under award numbers U01DA041022, U01DA041025, U01DA041028, U01DA041048, U01DA041089, U01DA041093, U01DA041106, U01DA041117, U01DA041120, U01DA041134, U01DA041148, U01DA041156, U01DA041174, U24DA041123, and U24DA041147.

ADVERSE INFANT AND CHILD OUTCOMES BY CONTINUED USE OF ALCOHOL AND OTHER SUBSTANCE USE DURING PREGNANCY AND 12-MONTH POSTPARTUM

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: The current report aimed to examine adverse effect of combined use of alcohol and other substance during pregnancy and 12-month postpartum on infant growth outcomes.
Methods: Data for the cross-sectional study were derived from a prospective study of mother-infant pairs enrolled in the Drakenstein Child Health Study (DCHS), conducted in Western Cape, South Africa. A total of 507 women who are pregnant responded to a question of whether she used alcohol in the past three months. Univariate and multivariate analyses were conducted to compare infant height and weight and standardized stunting scores during 12-month postpartum among three groups: Those with combined use of alcohol and tobacco both during pregnancy and at 12-month postpartum (Group 1: n = 43); those with combined use of substance including tobacco and cannabis but no alcohol both during pregnancy and at 12-month postpartum (Group 2: n = 71); and those with use of substance and/or alcohol either but not both during pregnancy and at 12-month postpartum (Group 3: n = 240).
Results: Univariate analyses of 3-group comparisons showed statistical significances ($p<.05$) in infant weight and height at 12-month but not 6-week timepoints. All timepoints for standardized stunting scores (birth, 10-week, 14-week, 6-month, 9-month, 12-month) showed statistical significances. Pairwise comparisons showed that Group 1 generally showed the worst outcome followed by Group 2 and Group 3. After adjusting for the covariates, all timepoints for standardized stunting scores and infant height at 12-month remained statistical significances ($p<.05$), while infant weight at 12-month was no longer statistically significant ($p=0.10$).
Conclusions: Much emphasis in substance and alcohol use treatment need to be made to distinguish education and intervention contents focused on combined use of substance and alcohol throughout pregnancy and first year postpartum including providing proper maternal and infant care for women in substance and alcohol use treatment.

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MISCONCEPTIONS TOWARD MEDICATION FOR OPIOID USE DISORDER AMONG PREGNANT AND POSTPARTUM PEOPLE

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Pregnant and post-partum people (PPP) who use opioids experience higher rates of parental morbidity, preterm labor, and stillbirth than those who do not. Although medication for opioid use disorder (MOUD) is associated with improved neonatal and post-partum outcomes, MOUD utilization among PPP has remain unchanged for nearly 30 years due to stigma and misconceptions associated with MOUD. The current exploratory study examined general and pregnancy-related MOUD misconceptions among PPP who use opioids.
Methods: Participants (n = 33) were PPP receiving MOUD at a Midwestern clinic. Participants reported beliefs about common MOUD misconceptions in four categories: efficacy, health impact, societal impact, and long-term use. They also responded to items regarding MOUD's safety for PPP generated by the research team based on previous qualitative findings. Analyses examined the association of misconceptions with subjective norms and self-efficacy toward MOUD.
Results: PPP reported low levels of MOUD misconceptions, particularly regarding efficacy. However, misconceptions about MOUD use for PPP varied. For example, 76% of PPP agreed that MOUD use was safe during pregnancy, whereas 72-84% reported misconceptions about the impact of MOUD on neonatal abstinence syndrome. Of the general misconceptions, only those about efficacy were inversely associated with subjective norms and self-efficacy ($r = -0.68$, $p < .001$; $r = -.91$, $p < .001$). Misconceptions about MOUD for PPP were also associated with lower subjective norms for using MOUD ($r = -.37$, $p < .05$).
Conclusions: Misconceptions about MOUD's efficacy and safety pre- and peri-natally are associated with lower subjective norms and self-efficacy for MOUD use, which may contribute to low MOUD utilization and retention among PPP. Findings emphasize the importance of assessing and mitigating MOUD misconceptions among PPP, even those utilizing MOUD. Future research should examine stigma and misconceptions among PPP without a history of MOUD use to clarify individual barriers to utilization.
Financial Support: K02 DA043657, 1H79TI081697, KL2 TR002346

ORAL COMMUNICATION: NICOTINE CO-USE

NEUROANATOMICAL CORRELATES OF CIGARETTE SMOKING SEVERITY IN PATIENTS WITH OPIOID USE DISORDER – A VOXEL-BASED MORPHOMETRY STUDY

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: Tobacco smoking and opioid use disorder (OUD) significantly impact brain structure, including reducing brain gray matter volume (GMV). Although OUD and tobacco smoking are strongly comorbid, most prior structural brain imaging research on OUD did not take smoking severity into consideration. Moreover, the combined effect of smoking and OUD on GMV remains unknown. This study aimed to examine: (1) the difference in brain GMV between OUD and non-OUD individuals with comparable smoking severity; and (2) the differential effect of smoking severity on brain GMV between individuals with and without OUD.
Methods: Sixty daily cigarette smokers with OUD (CS-OUD; 37 male, 23 female, 29.53±8.87 years old) and 56 daily smokers without OUD (CS; 31 male, 25 female, 30.09±10.81 years old) completed a T1-

weighted structural magnetic resonance imaging scan. The two groups were matched for age, sex, and smoking severity (3–40 cigarettes per day). Voxel-based morphometry analysis was performed to test group difference (CS-OUD vs. CS) and the interaction between group and smoking severity. Significant regions were identified at cluster-level corrected $p<0.05$.
Results: Compared to the CS group, the CS-OUD group had higher GMV in the occipital cortex and lower GMV in the frontal cortex, temporal cortex, and nucleus accumbens. There was a significant interaction between group and smoking severity on GMV in the medial orbitofrontal cortex (mOFC), such that heavier smoking was associated with lower mOFC GMV in the CS-OUD but not CS individuals.
Conclusions: OUD is associated with increased occipital GMV and reduced fronto-temporal and striatal GMV that cannot be accounted for by the severity of comorbid tobacco smoking. Having OUD may exacerbate the effect of tobacco smoking on the GMV of the mOFC, a region that plays a key role in reward processing and decision-making.
Financial Support: This work was supported by the Commonwealth of Pennsylvania CURE grant SAP#4100055577 (Childress) and the following National Institutes of Health grants: DA051709 (Shi), DA024553 (O'Brien), DA028874 (Childress), DA036028 (Langleben) and AA026892 (Wiers).

EFFECTS OF Δ9-TETRAHYDROCANNABINOL (THC) ON NICOTINE SELF-ADMINISTRATION IN A RODENT CO-ABUSE MODEL

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Drug Interactions
Abstract Detail Animal Study
Abstract Category Original Research
Aim: This study evaluated the effects of post-session and pre-session administration of Δ9-tetrahydrocannabinol (THC) on intravenous nicotine self-administration. We hypothesized that nicotine in combination with THC enhances reinforcing effects compared to those of either substance alone.
Methods: Prior to initiation of nicotine self-administration, male and female rats were administered vehicle, 3 mg/kg THC, or 30 mg/kg THC (n=8/sex/group) daily to represent non-THC use, or dual use with light or heavy THC use, respectively. Rats were then trained to self-administer nicotine with continued daily administration of THC or vehicle 3 hrs post-session. The nicotine dose-effect curve was then determined with THC administered pre-session to represent chasing THC with nicotine. A follow up study was conducted to determine how THC affects responding for food. Methods were the same as the nicotine self-administration study except that nicotine was replaced with sucrose pellets.
Results: Non-THC users self-administered more nicotine than dual users throughout acquisition ($p>0.05$). In non-THC users, pre-session THC dose-dependently shifted the nicotine dose-effect curve downward, whereas a low dose of pre-session THC increased nicotine self-administration in light THC users. In heavy THC users, nicotine self-administration was suppressed, regardless of whether rats received pre-session THC. In the food study, post-session THC did not significantly alter pellets earned during acquisition ($p>0.05$). Pre-session THC dose-dependently decreased pellets earned for non- and light THC users.
Conclusions: Results suggest that moderate and high doses of THC administered pre- or post-session may decrease nicotine's reinforcing effects in this model. The effects of high doses of pre-session THC may also be due to locomotor suppression. Post-session daily THC had a much smaller effect on food than nicotine self-administration; however, rats earned considerably more food reinforcers than nicotine infusions. Hence, the effects of daily post-session THC on responding for a reinforcer may be rate-dependent versus reinforcer dependent.
Financial Support: NIH Grant R33DA044377

CHRONIC ADMINISTRATION OF SYNTHETIC CONTRACEPTIVE HORMONES ALTERS NICOTINE CONSUMPTION IN AN ETHANOL CO-USE MODEL IN OVARY-INTACT FEMALE RATS

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Drug Category Nicotine/Tobacco

Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Tobacco and alcohol use disorders (TUD and AUD, respectively) are tremendous health liabilities, and co-use of these substances is highly prevalent in the United States. Women-specific risk vulnerabilities have been identified, as endogenously cycling ovarian hormones can impact frequency of binge drinking as well as cigarette craving. However, the impact of exogenous synthetic hormones commonly found in oral contraceptives (OCs) may influence motivation for alcohol and nicotine. OCs contain synthetic forms of estrogen (e.g., ethinyl estradiol, or EE) and/or progesterone (e.g., levonorgestrel, or LEVO). Despite the influence of hormones on addiction vulnerability, little is known regarding OC impacts on nicotine and alcohol co-use. Here we determined the influence of EE and LEVO on nicotine and ethanol (EtOH) intake in rats. We hypothesized that female rats given EE+LEVO will show increased nicotine and EtOH consumption as compared to vehicle or LEVO-only treatment.
Methods: Ovary-intact Long Evans female rats (N=36) first underwent a drinking in the dark paradigm (DID) in which they received water or 10% EtOH for 4-hrs. Following DID, rats underwent jugular vein catheter surgery along with daily subcutaneous injection of either LEVO (0.6 µg/0.1 mL), EE+LEVO (0.3/0.6 µg/0.1 mL), or vehicle (sesame oil). Rats then resumed DID in the morning and began nicotine self-administration (SA; 0.06 mg/kg/infusion, FR1) in the afternoons.
Results: EtOH-naïve females receiving EE+LEVO consumed more nicotine as compared to LEVO-only (Welch's t test, $p=0.022$) and vehicle groups (Welch's t test, $p=0.017$). In contrast, EtOH-experienced females treated with EE+LEVO consumed more nicotine than vehicle (Welch's t test, $p=0.004$), with a trending increase from LEVO-only treated females (Welch's t test, $p=0.053$). Further, EtOH-experienced vehicle rats consumed less nicotine overall than EtOH-naïve vehicle rats (Welch's t test, $p<0.0001$).
Conclusions: Contraceptive hormones mediate nicotine consumption in a nicotine and EtOH co-use model, and EtOH SA prior to nicotine SA decreases nicotine consumption.
Financial Support: University of Kentucky Ignight Research Grant

EFFECTS OF ETHANOL CONSUMPTION IN GROUP AND ISOLATE HOUSED ADOLESCENT MALE RATS ON ADULT DRINKING AND ETHANOL-NICOTINE CO-USE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Alcohol use often begins in adolescence and can lead to increased susceptibility to AUD in adulthood. Stress during adolescence can also prompt substance use disorders later in adulthood. This study determined if exposure to ethanol (EtOH) during adolescence in rats that undergo social isolation stress alters the trajectory of alcohol and nicotine intake during adulthood.
Methods: Group and isolate housed male Sprague-Dawley rats (n=24) were exposed to 0.2% saccharin (w/v)/20% EtOH (v/v) using an intermittent 24-hour 2-bottle choice during adolescence (PND 28-61); control rats received water only. In adulthood, rats (n=12) underwent 2-bottle choice sessions (PND 73-86), then were trained to self-administer nicotine (0.03 mg/kg/infusion) with EtOH and water concurrently available. The FR requirement was incrementally increased across sessions from FR1 to FR135.
Results: A two-way ANOVA revealed an effect of housing on EtOH intake during adolescence ($F(1,10) = 5.069$, $p = 0.0481$), with isolate rats drinking more than group rats ($t(26) = 9.627$, $p < 0.0001$). In the adult 2-bottle choice, there was a significant increase in EtOH intake in isolate EtOH rats compared to isolate H2O rats ($t(12) = 2.054$, $p = 0.0312$). During the co-use phase, a two-way ANOVA revealed a significant effect of FR requirement, with EtOH intake increasing ($F(2.304, 9.216) = 9.247$, $p = 0.0053$) and nicotine intake decreasing ($F(2.176, 8.706) = 22.32$, $p= 0.0003$) as the FR requirement was raised. There was also a treatment group x FR interaction ($F(33,44) = 1.80$, $p= 0.0344$), with isolate EtOH rats drinking more than group EtOH rats, but only at high FR values; no group differences were observed with nicotine intake.
Conclusions: These preclinical results indicate that stress paired with EtOH exposure in adolescence detrimentally affects the trajectory of adult EtOH use when given alone or co-used with nicotine.
Financial Support: NIH grant R01 AA025591

ORAL COMMUNICATION: WHAT IS THE ROLE OF DIET IN SUDS?

ENERGY METABOLISM-PARKIN LINK IN METHAMPHETAMINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Animal Study
Abstract Category Original Research
Aim: In the height of the opioid crisis in our country, deaths from methamphetamine (METH) overdose are on the rise, and there is no FDA-approved medication for METH use disorder. New pharmacotherapies are needed, especially for people who abuse METH heavily and are at high risk for METH overdose. Risk for developing METH use disorder has a genetic component that is not fully understood. Our recent study has implicated parkin gene and parkin protein deficit in vulnerability to abuse METH. Specifically, we showed that parkin gene knockout rats (Park2-/- rats) self-administered more METH whereas rats overexpressing parkin in the nucleus accumbens (PO-NAc rats) self-administered less METH than their wild-type counterparts in an extended-access METH self-administration model of heavy METH abuse (Transl Psychiatry, 2021, 11:293). Molecular mechanisms downstream of Park2 knockout or overexpression that led to this predisposition or "resilience" to heavy METH abuse are not known.
Methods: We have addressed this knowledge gap by comparing accumbal proteomes from drug-naive Park2-/-, PO-NAc and wild-type rats, as well as from rats with parkin deficit or excess in the dorsal striatum (DST), using the state-of-the-art proteomics.
Results: Pathways that significantly changed in opposite directions in the NAc in Park2-/- and PO-NAc rats as compared to wild-type controls were energy metabolism pathways. Analysis of dorsostriatal proteomes from Park2-/-, PO-DST, and wild-type rats revealed similar changes between the genotypes, with parkin deficit leading to negative regulation of selective energy metabolism pathways and parkin overexpression leading to positive regulation od selective energy metabolism pathways.
Conclusions: METH has been shown to cause mitochondrial dysfunction and decrease energy production in striatal areas of the brain; therefore, our results suggest that the parkin overexpression-mediated attenuation of heavy METH abuse occurs via increasing energy metabolism in ventral and dorsal striatum.
Financial Support: Yale/NIDA Neuroproteomics Center Pilot Research Project Grant.

THE ASSOCIATION BETWEEN BRAIN GLUTAMATE AND SLEEP EFFICIENCY FOLLOWING A KETOGENIC DIET INTERVENTION IN INDIVIDUALS WITH ALCOHOL USE DISORDER

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Drug Category Alcohol
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Chronic alcohol use induces sleep impairments that promote continual alcohol use and hinder recovery progress. We have previously shown the effectiveness of a ketogenic diet (KD) in curbing alcohol withdrawal and craving. In this secondary analysis of the KD intervention trial in individuals with alcohol use disorder (AUD), we aimed to (1) examine the effects of KD on sleep measures and (2) associate cingulate glutamate concentration with KD-induced changes in sleep.
Methods: AUD individuals undergoing detoxification were randomized to receive KD (n=19) or standard American diet (SA; n=14) for three weeks. Total sleep time (TST [hrs.]) were measured weekly by self-report, GENEActive sleep accelerometer, and X4 Sleep Profiler ambulatory device, which additionally measured Sleep Efficiency [%] and Wake After Sleep Onset (WASO [min]). Weekly 1H magnetic

resonance spectroscopy scans were performed, and cingulate glutamate levels were analyzed relative to creatine.
Results: TST throughout 3 weeks detoxification decreased with KD (subjective: F(1,31)=4.3, p=0.046; GENEActive: F(1,22)=5.5, p=0.028; Sleep Profiler: p=0.54) and improved with abstinence (GENEActive only: F(1,22)=7.1, p=0.014). There was a trending diet effect of KD in lowering WASO (F(1,30)=3.7, p=0.065). Sleep efficiency improved with abstinence (F(2,60)=8.1, p=0.002), but did not show effects of diet or diet-by-abstinence interaction. Week 1 cingulate glutamate levels correlated positively with sleep efficiency (r=0.54, p=0.001), and negatively with WASO (r=–0.43, p=0.015) in KD and SA combined, but not with measures of TST. KD-induced changes in glutamate levels during the 3-weeks intervention was not significantly associated with any other sleep measurements.
Conclusions: A KD intervention appears not to have beneficial effects on TST or Sleep efficiency in AUD undergoing detoxification. Cingulate glutamate levels correlated with sleep efficiency in week 1, but did not mediate diet-induced changes in sleep. Given the well-established associations between sleep and alcohol relapse, further elucidation of KD's impact on sleep is warranted in AUD individuals.
Financial Support: National Institute on Alcohol Abuse and Alcoholism

KETOGENIC MANIPULATIONS AS TREATMENT OF ALCOHOL WITHDRAWAL SYMPTOMS

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Drug Category Alcohol
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: It has been shown that during alcohol intoxication, brain glucose metabolism is decreased while brain acetate metabolism is increased. This metabolic shift persists during abstinence, where decreased acetate availability could lead to a state of energy depletion in the brain, which in turn may contribute to or worsen alcohol withdrawal symptoms. This study aims at testing the efficacy of ketogenic treatments as an alternative source of energy, investigating their potential to rescue psychiatric and neurochemical alterations during long-term alcohol withdrawal.
Methods: Female C57BL/6JRj mice, tested in cohorts (randomized block design) were intermittently exposed to alcohol vapors or air for three weeks. From the last week of alcohol exposure, mice were fed either control diet (CD, n=12), ketogenic diet (KD, n=12) or diet supplemented with ketone ester (KE, n=12). Withdrawal symptoms were assessed over a period of four weeks using a battery of behavioral test, comprising alcohol self-administration, anhedonia (saccharin preference), hyperalgesia (hot-plate), anxiety-like (light-dark, zero maze) and depressive-like disturbances (tail suspension). Brain inflammation was measured by cytokine assay and monoamine, GABA and glutamate levels in the hippocampus and striatum, as well as positive ions content in the cerebellum, were assessed by HPLC
Results: Alcohol-exposed mice fed either KD (means 81.8; 89.0) or KE (means 80.8; 89.5) displayed increased saccharin preference when compared to alcohol-exposed mice fed CD (means 52.6; 53.2), measured after one and three weeks of abstinence, respectively (both $p<0.01$). Similarly, KD-fed alcohol-exposed mice showed a trend for increased (normalized) light/dark crossings (mean 94.0) compared to alcohol-exposed CD-fed mice (mean 77.0; p=0.0532). Results are preliminary from two out of three cohorts.
Conclusions: Our findings show promise for ketogenic treatments to rescue some alcohol withdrawal symptoms in mice, not only in early detoxification, but also during prolonged abstinence.
Financial Support: Independent Research Fund Denmark

SEX DIFFERENCES IN CANNABINOID-MEDIATED ENERGY HOMEOSTASIS

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Drug Category Cannabis/Cannabinoids
Topic Sex/Gender Differences
Abstract Detail Human

Abstract Category Original Research
Aim: The interplay of sex hormones and the cannabinoid system has been established in several physiological process. Evidence on modulation of energy homeostasis by cannabinoids, however, is primarily derived from male models. This is an important gap in the literature since regulation of energy balance shows significant sex differences. Here, we use male and female mice lacking cannabinoid-1 (CB1) receptors globally or peripherally in the adipose tissue to characterize sex differences in the metabolic health effects of cannabinoids.
Methods: All mice (n = 12/group) were on C57BL background because of their susceptibility to diet-induced obesity. Seven-week-old wild-type (WT), whole body CB1 knockout and adipose tissue CB1 knockout mice were fed ad libitum either with a high at diet (HFD) with 45% of energy from fat or a low-fat diet (LFD; 10% of energy from fat) for 6 weeks. Body weight was recorded weekly. A subset of mice from each experimental group were housed individually for 1 week in TSE metabolic cages to continuously measure food intake, locomotion and parameters of indirect calorimetry. At the conclusion of the study, a subset of mice were fasted for 5 hours early in the morning and then glucose (2g/kg) was administered via intraperitoneal injection to assess glucose clearance.
Results: Consistent with previous studies, male mice lacking CB1 receptors globally or in the adipose tissue were less likely to gain weight when fed with HFD compared to WT mice. These differences were less pronounced among female mice. Additionally, there were no appreciable differences in food intake, locomotor activity or glucose clearance among female mice in the three groups.
Conclusions: These data suggest that the cannabinoid system alters energy balance centrally and peripherally in a sex-specific way. Further analyses examining the sex-specific effects of CB1 receptor deletion on adipose tissue biology will be presented in June meeting.
Financial Support: R00AT009156 and MICHIGAN STATE UNIVERSITY

WEDNESDAY, JUNE 15, 2022

ORAL COMMUNICATION: GENETICS OF SUDS II

COCAINE SELF-ADMINISTRATION INDUCES SEX-DEPENDENT PROTEIN EXPRESSION IN THE NUCLEUS ACCUMBENS

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Drug Category Stimulants
Topic Genetics/Proteomics/Metabalomics
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Outlining the neural mechanisms of drug addiction has been a focus of preclinical work for the past few decades; however, this research has overwhelmingly used male subjects. Although both males and females become addicted to cocaine, there is evidence emerging that behavioral and biological mechanisms behind addiction may be different between sexes. Clinical work has shown that females transition to addiction faster, consume more cocaine, and have greater difficulty remaining abstinent and many of these findings have been replicated in preclinical models, suggesting biological mechanisms play a role in these differences.
Methods: Male and female mice (n=5 per group) self-administered cocaine or saline for 10 days and tissue was collected on day 10 to assess the sex-specific protein expression patterns induced by cocaine self-administration using quantitative mass spectrometry.
Results: We saw unique protein expression profiles between males and females in the nucleus accumbens at baseline and showed that cocaine self-administration induces non-overlapping protein expression patterns in significantly regulated proteins in males and females. Additionally, we showed that while cocaine self-administration differentially regulated protein expression between males and females, it also acted to reduce the basal differences in protein expression.
Conclusions: These data suggest that an interaction between basal biological differences and differential regulation of targets caused by drug self-administration could be playing a role in sex differences in

addiction and provide evidence that treatment of drug addiction may need to take a sex-specific focus both behaviorally and biologically.
Financial Support: This work was supported by the NIH (DA042111 and DA048931 to E.C.; DA044308, DA-049568, and DA-051551 to D.K.; DA041838 to A.L. as well as funds from the Brain and Behavior Research Foundation in the form of a Young Investigator Grant (to E.S.C., and D.D.K.). the Whitehall Foundation (to ESC), and the Edward Mallinckrodt Jr. Foundation (to E.S.C.). The Orbitrap Fusion mass spectrometer and the Offline UPLC utilized were supported in part by NIH SIG grants S10OD019967-0 and 1S10ODOD018034-01, respectively, and Yale School of Medicine. This work was supported by the Yale/NIDA Neuroproteomics Centre Grant DA018343.

WITHIN SUBJECT CROSS-TISSUE ANALYSES OF EPIGENETIC CLOCKS IN SUBSTANCE USE DISORDER POSTMORTEM BRAIN AND BLOOD

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: An accelerated biological aging in patients with substance use disorders (SUD), is one of the main contributors to adverse outcomes in SUD. The evaluation of epigenetic clocks -accurate DNA methylation estimators of biological aging- has been limited to blood in patients with SUD. Therefore, we aimed to evaluate the impact of epigenetic aging in the brain of individuals with SUD and compare brain and blood epigenetic clocks to assess the use of blood measures as proxies of brain measures.
Methods: We collected postmortem brain (Brodmann Area 9) and peripheral blood samples from individuals with SUD (n=42), including alcohol (n=10), opioid (n=13), stimulant use disorder (n=19), and controls (n=10). Samples were obtained from The University of Texas with Institutional Review Board approval. The DNA methylation profile of each sample was assessed and used to calculate the following epigenetic clocks: DNAmAge, DNAmAgeHannum, DNAmPhenoAge, DNAmGrimAge, and DNAmTL. Later, for these epigenetic clocks we evaluated: 1) differences between individuals with and without SUD in brain and blood, separately using a linear regression model; 2) cross-tissue differences with a linear regression model, and 3) brain-blood correlations using Pearson tests.
Results: We found a higher DNAmPhenoAge (p-value=0.006) and lower DNAmTL (p-value=0.03) in blood from individuals with SUD compared to controls. SUD subgroup analysis showed a lower brain DNAmTL in individuals with alcohol use disorder, compared to those with stimulant use disorder and controls (p-value=0.02). Cross-tissue analyses indicated a lower blood DNAmTL and a higher blood DNAmGrimAge compared to their respective brain values in the SUD group.
Conclusions: This is the first cross-tissue study investigating the relationship between brain and blood epigenetic clocks from individuals with SUD. This study highlights the relevance of tissue specificity in epigenetic aging studies and suggests that peripheral measures of epigenetic clocks in SUD may depend on the type of drug used.
Financial Support: This study was funded by the National Institute on Drug Abuse (NIDA) and the Fogarty Foundation (R01DA044859 to CWB). GRF is funded by the National Institute of Mental Health (NIMH, K01 MH121580).

TRANSCRIPTOMICS IN THE PREFRONTAL CORTEX OF COMORBID DEPRESSION AND ALCOHOL USE DISORDER

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Drug Category Alcohol
Topic Genetics/Proteomics/Metabalomics
Abstract Detail Human

Abstract Category Original Research
Aim: Comorbid major depressive disorder (MDD) and alcohol use disorder (AUD) is common in clinical populations and result in a worse course of illness than is observed in either along. Recent studies have demonstrated substantial genetic overlap between the diseases. Despite this, these individuals are often excluded from studies or either of the two diseases. The prefrontal cortex, the dorsolateral (dlPFC) and orbitofrontal (OFC) regions in particular, includes neural circuits disrupted in the disease. This work aimed to identify differences in gene expression in the prefrontal cortex associated with comorbid AUD and MDD compared to MDD alone.
Methods: The dlPFC and OFC were isolated from 43 demographically similar individuals: controls (n=9), depression (n=21), and depression with comorbid AUD (n=13). Total RNA was isolated and next generation sequencing was performed using an Illumina NextSeq 500 with a 150 bp paired-end protocol. Data was processed using multiple bioinformatic pipelines, cuffdiff and DESeq2, and functional enrichment was performed with Ingenuity Pathway Analysis.
Results: 203 genes were differentially expressed (FDR=0.05) in AUD-comorbid depression compared to depression alone, including CASP4 (caspase 4), FGFR3 (regulating cell growth and proliferation), CXCL10 (secreted in response to IFN-γ), interleukins (IL-2,-4,-6,-8,-9,-10,-15,-17,-32), TNFRSF1A (TNFα receptor), and NFκB1A (inflammatory function). Functional enrichment analysis demonstrated overlap, but not unity, in category enrichment, notably in many signaling pathways regulating cellular response to cytokine stimulus and cytokine-mediated signaling pathways.
Conclusions: These results suggest an important role for neuroinflammation in depression that is significantly exacerbated with comorbid alcohol use disorder. These represent human cohort studies and are necessarily not longitudinal so it is not possible to identify whether alcohol use is driving the gene expression differences in individuals with depression or if existing gene expression differences in a subset of individuals with depression are leading to a vulnerability to alcohol use disorder.

EMERGING EVIDENCE OF FEASIBILITY AND BEHAVIOR CHANGE ASSOCIATED WITH FULLY-REMOTE DELIVERY OF A GENETICALLY-INFORMED SMOKING CESSATION INTERVENTION

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Drug Category Nicotine/Tobacco
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: Genetic variation in nicotinic receptor subunits explains differences in smoking behaviors and risk of smoking-related diseases. Despite promising findings in recent proof-of-concept testing, it remains unknown whether returning genetic susceptibility results can motivate smoking cessation and personalize treatment. The potential mechanisms of behavior change, as well as the optimal delivery approach in an increasingly virtual healthcare landscape, also warrant investigation.
Methods: To date, we have enrolled 81 adult participants who smoke in a fully-remote randomized controlled trial including genetic testing via 23andMe, Zoom-based delivery of a genetically-informed risk feedback tool (RiskProfile) or active comparator (brief cessation advice), and 30-day and 6-month follow-ups.
Results: Feasibility: We have successfully obtained genetic test results for 99% of participants who mailed a DNA sample to 23andMe, with an average turnaround of 18 days from DNA sampling to creation of the personalized RiskProfile ready for intervention. These efficiencies, along with an established protocol for completing all study visits remotely, has yielded robust participant engagement and retention.
Behavior change: As hypothesized, interim analyses (n=61 with completed 30-day follow-up) with repeated-measures ANOVA controlling for baseline cigarettes per day (CPD) yield promising effect size estimations (e.g., partial eta-squared=.032, small-to-medium effect size), indicating clinically meaningful behavior change characterized by reductions in average CPD of 2.6 in the RiskProfile intervention group versus 1.1 in the active comparator group. Importantly, 42% in the intervention group versus 17% in the comparator group sought medication treatment for smoking. Increases in perceived importance of tobacco treatment, and decreases in perceived self-stigma, appear to be particularly promising mechanisms of behavior change.

Conclusions: In this ongoing fully-remote trial, we have (1) significantly reduced access-related barriers to participation, (2) protected the health and safety of participants and research staff by avoiding potential COVID exposures, and (3) generated emerging evidence of behavior change mechanisms leading to reduced cigarette smoking.
Financial Support: NIH/NIDA K12DA041449 and R34DA052928

ORAL COMMUNICATION: INTERSECTIONALITY BETWEEN SUDS AND SUICIDALITY

PRINCIPAL COMPONENT REGRESSION ANALYSIS OF FAMILIAL PSYCHIATRIC HISTORIES AND SUICIDE RISK FACTORS AMONG ADULTS WITH OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Patients with opioid use disorder (OUD) are at elevated risk of suicide. This study explores familial psychiatric risk factors that are closely linked to suicide risk among patients with OUD as measured by the Family History Assessment Module (FHAM). We hypothesize that family histories of suicidal behaviors will be positively correlated with OUD patient presentation of current suicidal behaviors.
Methods: Baseline data came from participants (N=386), including both sexes, who took part in a larger digital intervention study designed for adults with OUD. To analyze the covariance between 11 items related to FHAM, principle component analysis (PCA) was applied to infer principal components (PC) scores. Logistic regressions were conducted to quantify the associations between PC scores and mental health symptoms and behaviors, including lifetime suicide attempts.
Results: PCA revealed that first 3 PCs of 11, could account for 58% of the total variance of the items within the baseline data (N=386). PC1 may be interpreted as a measure of covariance for those who have a family history of seeking professional help and hospitalizations for substance use issues. PC2 is a measure of family history with serious mental illness. Lastly, PC3, is a measure of family history and its relation to attempted suicide and deaths by suicide. Logistic regression results show that PC1 was positively associated with lifetime suicidal attempts (AOR: 1.65, 95% CI: 1.32- 2.06), severe depression (AOR: 1.40, 95% CI: 1.07- 1.83), and severe anxiety (AOR: 1.62, 95% CI: 1.21- 2.17). No significant association for present suicide risk was observed for PC2 or PC3.
Conclusions: Our findings show that present suicide risk is strongly associated with an array of familial mental health issues. However, our results show that a family history of suicide attempts and death by suicide has less bearing on present suicide risk in the sample of OUD patients.
Financial Support: Substance Abuse and Mental Health Services Administration (DHHS)
Grant Number:1H79TI081687-02

CANNABIS USE IS ASSOCIATED WITH DEPRESSION SEVERITY AND SUICIDAL BEHAVIOR IN THE NATIONAL COMORBIDITY SURVEY – ADOLESCENT SUPPLEMENT

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Drug Category Cannabis/Cannabinoids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: The aims of this study are to 1) investigate the prevalence of MDD in adolescents with lifetime cannabis use and 2) explore the association of lifetime cannabis use with MDD severity and symptomatology.
Methods: Data are from the National Comorbidity Survey-Adolescent Supplement (n=10,123), a nationally representative survey of adolescents aged 13 to 18 years old. Analyses in SAS accounted for the complex

survey design. Weighted logistic regression and ordinal regression analyses were conducted adjusting for sociodemographic variables associated with lifetime cannabis use and/or DSM-IV MDD (age, gender, race/ethnicity, and region).
Results: Of the 2,281 adolescents reporting lifetime cannabis use, 432 (18.9%) met criteria for a lifetime diagnosis of MDD, compared to 8.9% of adolescents who never used cannabis ($p<0.0001$). Severe depression was also more prevalent in adolescents with lifetime cannabis use (6.8% vs 1.8%, $p<0.0001$). Adolescents with lifetime cannabis use had 2.1 times higher odds of having mild/moderate depression (aOR 95% CI 1.69, 2.53) and 3.1 times higher odds of having severe depression (aOR 95% CI 2.31, 4.75) than no depression, compared to adolescents who never used cannabis. Similarly, adolescents who used cannabis in the past 12 months had higher odds of a mild/moderate or severe depressive episode within that time, compared to adolescents who did not use cannabis (aOR 2.06 and 2.83, respectively). Among adolescents with a lifetime diagnosis of MDD, changes in appetite ($p=0.021$), suicidal ideation ($p=0.0027$), and suicide attempt ($p=0.030$) were associated with lifetime cannabis use. There were no significant differences in the prevalence of depressed mood, anhedonia, sleep, psychomotor agitation or retardation, fatigue, worthlessness, concentration, guilt, or suicide plan.
Conclusions: MDD is more prevalent among adolescents with lifetime cannabis use with higher odds for severe MDD. Of concern, lifetime cannabis use is also associated with a higher prevalence of suicidal ideation and suicide attempt.
Financial Support: K12DA000357

GENDER DIFFERENCES IN DRUG-RELATED SUICIDE DEATHS IN THE U.S., 1999-2019

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Drug Category Other, Benzodiazepines, Antidepressants, Alcohol, Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Drug use has been associated in different countries with suicide deaths. There have been markedly gender differences in both substance use and suicidal behaviors. Thus, it is important to explore gender differences in drug-related suicide deaths.
Methods: We examined drug-related suicide deaths identified in the National Vital Statistics System (NVSS) from 1999 to 2019. They were identified using the ICD–10 underlying cause-of-death codes U03, X60–X84, and Y87.0. Drug involvement was detected using the ICD-10 following codes for all drugs (T36-T50); and then by type of drug, as follows: opioids (F16.0; T40.0-T40.4, T40.6); stimulants (F14.0; F15.0; T40.5, T43.6); benzodiazepines (F13.0; T42.4); antidepressants (T43.0-T43.2); alcohol (F10.0; T51), which were the most popular drugs involved in the suicides in this sample. Age-adjusted suicide death rates were calculated using the direct method and the 2000 U.S. standard population. Initially, we stratified the number, percentage, age-adjusted suicide rates per 100,000 and their 95% confidence intervals by gender for the entire period of 1999-2019. Finally, gender-stratified yearly-trend curves for age-adjusted rates of drug-related suicide deaths from 1999 to 2019 were plotted, stratified by type of drug involved.
Results: During the entire period, 8.6% of all the suicide had any drug involvement (n = 68,260; Age-Adjusted Death Rate = 1.1 per 100,000). Higher female prevalence was found among suicides with drug involvement (49.2%) than those without (21.3%). Trend curves showed that antidepressant and alcohol involvement in suicides were consistently higher among females and males, respectively (78% and 62% higher in 2019). Since 2011, benzodiazepine involvement was higher among females (37% higher in 2019). Opioid involvement was quite similar among both genders during the entire period.
Conclusions: Females are at higher risk than males for antidepressant- and benzodiazepine-related suicides. Males are at higher risk than females for alcohol-related suicides. Apart from opioids, gender-tailored drug-related suicide prevention strategies should be taken.
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BE WELL RVA (RICHMOND, VIRGINIA) SUICIDE PREVENTION AND DOMESTIC VIOLENCE PROJECT

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Integrating behavioral and primary health care in the same setting where individuals receive ongoing services, and where they are comfortable, is a much-desired solution. The Richmond Behavioral Health Authority (RBHA), a behavioral health services provider in Richmond, has significantly expanded its integrated health care services by incorporating primary care, to include suicide prevention and domestic violence interventions. The Be Well RVA Project is a suicide and domestic violence prevention and intervention initiative that is based in our integrated primary/behavioral health services center. With a grant from the Substance Abuse and Mental Health Administration (SAMHSA), Be Well RVA provides: Community Prevention; Care Coordination with local providers and emergency rooms; Clinical services aimed at addressing immediate behavioral health needs, with a specific focus on suicide and domestic violence; and wrap-around support services in addition to connections with various community service providers.
Domestic violence (DV) survivors have higher than average rates of suicidal thoughts as well as high rates of substance use disorders. As many as 23% of survivors have attempted suicide compared to 3% among populations with no prior DV exposure
Methods (Optional): Analysis and reporting of selected details of patient data collected over the past 16 months of the project will include a profile of the population served and health outcomes will be presented. We will examine the treatment outcomes of those who scored high on the DV screening, as well as examine their behavioral health diagnoses. Patients must meet the following criteria in order to participate in Be Well RVA: Significant risk of suicidal and/or domestic violence crisis; City of Richmond resident; Medicaid, uninsured, or underinsured; Eligible for services/receiving services at RBHA as evidenced by a behavioral health disorder; and be 25 years of age or older.
Results (Optional): This program description will include: 1) Challenges met and innovations initiated; 2) Details about populations served, including demographics and high-level outcome data; and 3) Challenges with regard to staffing, culture change, and billing.
Conclusions: The Be Well RVA project has led to a culture change in RBHA's approach to the delivery of primary care and behavioral health services that is more holistic, person-centered, and ideally meets the challenges of the future while improving outcomes for the people we serve.
Financial Support: This project was supported by federal grant funds.

ORAL COMMUNICATION: INFECTIOUS DISEASES AND SUDS

ASSOCIATION OF OPIOID AGONIST TREATMENT WITH MORTALITY OR REHOSPITALIZATION FOLLOWING INJECTION DRUG USE-ASSOCIATED BACTERIAL AND FUNGAL INFECTIONS: LINKAGE COHORT STUDY

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: Among people with opioid use disorder following hospital discharge with injecting-related bacterial or fungal infections, we assessed whether outpatient use of opioid agonist treatment (OAT; i.e. methadone or buprenorphine) was associated with decreased risk of death or infection-related rehospitalization.
Methods: We analyzed data from the Opioid Agonist Treatment Safety (OATS) Study, a population-based, retrospective linkage cohort including all people in New South Wales, Australia, who accessed OAT between 1 July 2001 and 28 June 2018. We included participants who survived a hospitalization with

injecting-related bacterial or fungal infections (i.e., skin and soft-tissue infection, sepsis/bacteraemia, endocarditis, osteomyelitis, septic arthritis, or epidural/brain abscess). Outcomes were all-cause death and rehospitalization for injecting-related infection. We used separate Cox proportional hazards models to assess associations between each outcome and OAT exposure, classified as time-varying by days on or off treatment. Covariates included participant demographics, comorbidities, prior substance-use related hospitalizations and incarceration, and index hospitalization characteristics.
Results: The study included 8,943 participants (mean age 39 ± 11 years; 34% women). The most common infections during participants' index hospitalizations were skin and soft-tissue (7,021; 79%), sepsis/bacteraemia (1,207; 14%), and endocarditis (431; 5%). Prevalence of OAT exposure was 48% on day 1, and participants had median 2 [IQR 0-5] switches on or off treatment during follow-up. Over median 6.56 years follow-up, 1,481 (17%) participants died and 3,653 (41%) were rehospitalized for injecting-related infections. OAT was associated with lower hazard of death (adjusted Hazard Ratio [aHR] 0.63, 95% confidence interval [CI] 0.57 - 0.70) and of rehospitalization (aHR 0.89, 95% CI 0.84 - 0.96).
Conclusions: Following hospitalizations with injecting-related bacterial and fungal infections, OAT is associated with reduced risk of death and recurrent infections among people with opioid use disorder. OAT should be offered and facilitated as part of a multi-component treatment strategy for injecting-related infections.
Financial Support: Canadian Institutes of Health Research; National Institutes of Health

COMORBIDITY BURDEN AND HEALTH CARE UTILIZATION AMONG PEOPLE WITH HIV AND SUBSTANCE USE DISORDER

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Drug Category Other, general substance use disorder
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: The improved life expectancy of people with HIV (PWH) in care has been accompanied by increased comorbidity burdens. Substance use disorder (SUD), a common comorbidity among PWH, may have a syndemic link with HIV infection and magnify comorbidity and health care burden. We aim to 1) determine the prevalence of SUD diagnosis among PWH and 2) assess the comorbidity burden and health care utilization by SUD status and patterns.
Methods: A virtual cohort of 61,313 people with HIV has been identified in OneFlorida, a statewide patient data repository in Florida, using a validated computable phenotype. The prevalence of SUD and commordibities in the Charlson comorbidity index (CCI) was estimated among this cohort using ICD codes. The CCI, the annual average number of any visits, inpatient, and emergency department (ED) visits were calculated and compared by SUD status.
Results: The lifetime prevalence of having any SUD among PWH was 52.1%. Specially, 8.2% had tobacco use disorder only, 13.9% had alcohol/cannabis/tobacco use disorder only, and 19.3% had any stimulant/opioid use disorder. Having SUD diagnosis among PWH were associated with higher CCI score; the odds of having each comorbid condition ranged from 1.47 for diabetes without complication to 3.73 for chronic pulmonary disease. Amongst SUD patterns, the association of having stimulant or opioid use disorder with higher CCI score was the strongest. Moreover, PWH with any SUD was associated with more inpatient and ED visits relative to PWH without SUD.
Conclusions: Higher comorbidity and health care utilization among PWH with SUD may create an additional burden for health care delivery as PWH age in the US. Patient-centered care coordination is needed especially those with stimulant or opioid use disorder.

BUILDING A STATEWIDE PEER NETWORK FOR HARM REDUCTION: OREGON'S PEER RECOVERY INITIATED IN MEDICAL ESTABLISHMENTS + HCV/HIV TESTING AND LINKAGE TO TREATMENT (PRIME+) PROGRAM

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Harm Reduction
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Oregon is widely affected by opioid and methamphetamine use and harms, including overdose and infections (such as hepatitis C) related to injection drug use. Oregon Health Authority (OHA) has funded organizations serving 24 of the 36 counties around the state to implement the PRIME+ peer program, employing peers with lived experience to engage people in need of support and link to resources, services, and care. The program builds on a research study (Oregon HOPE) to develop a rural peer model. PRIME+ peers engage people who are at varying stages of change, using a harm reduction approach. Participants are referred by hospitals/emergency departments and other medical settings, varied community organizations, and direct street outreach. This presentation will describe the state-level infrastructure needed to support the program, and implementation successes and challenges.
Conclusions: PRIME+ implementation and evaluation will improve understanding of peer-based interventions combining harm reduction, HCV testing, MOUD linkage, and peer support for people who use drugs. The following will be highlighted in the poster presentation:
• Describe a peer-based harm reduction intervention to promote HCV testing and support access to treatment among people who use drugs
• Describe a "no wrong door" approach for engaging people who use drugs in high-impact settings
• Discuss how peer support specialists with lived experience connect with people who use drugs to reach self-identified goals for health, well-being, and quality of life
• Describe lessons learned from implementation of statewide peer model, such as need for adequate supervision, considerations when supervising individuals in recovery from addiction, robust learning collaborative for ongoing training and professional development, respite program for peers when fatal and nonfatal overdoses occur, and developing an infrastructure that facilitates natural supports and interdependence between peers conducting this work across the state
Financial Support: This work was supported by SAMHSA grant #081716-02 and CDC grant # NU51PS005080

ORAL COMMUNICATION: COCAINE CLINICAL RESEARCH

COMPARISON OF SUBJECTIVE AND OBJECTIVE SLEEP IN A STUDY OF OREXIN ANTAGONISM FOR COCAINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The reciprocal relationship between cocaine use and sleep deficits underscores the importance of targeting sleep in treatment for cocaine use disorder (CUD), and accurately monitoring changes in sleep across time. Research shows a discrepancy between subjective and objective sleep among individuals with CUD, but this remains to be examined among individuals with CUD who are receiving an orexin antagonist that regulates sleep architecture. This study compared subjective and objective sleep outcome measures among individuals with CUD who received either the orexin antagonist suvorexant or placebo. Follow-up analyses explored moderating factors of measured sleep duration.
Methods: Non-treatment seeking adults with at least moderate CUD completed baseline measures of emotional and cognitive functioning. Male and female participants then received suvorexant (n=10) or placebo (n=10) daily for two weeks and wore actigraphy watches as an objective measure of total sleep duration. Further, participants completed a brief subjective measure of sleep duration. Generalized linear mixed modeling examined subjective and objective sleep duration as a function of the interaction between medication group and time. Follow up analyses evaluated potential moderating effects of psychosocial covariates on longitudinal changes in sleep duration.

Results: The interaction between group and time was not supported (p>.05) for subjective or objective sleep duration, nor were the main effects of time or group. Controlling for treatment group, several psychosocial factors were supported (p<.05) as moderators of change in objective sleep duration over time, including anhedonia, distress tolerance, trauma, and avoidance.
Conclusions: In the context of a clinical trial of an orexin antagonist for CUD, comparisons of objective and subjectively measured outcomes of sleep duration showed no differences. Objective, but not subjectively-reported sleep duration was associated with cognitive and emotional processes. Results provide guidance for methodological considerations in research targeting sleep among individuals with CUD.
Financial Support: Peter F. McManus Foundation (SDL) and the UTHealth McGovern Research Scholar Award (SDL).

PREGNENOLONE EFFECTS ON AUTONOMIC RESPONSE TO STRESS AND COCAINE CUE IN INDIVIDUALS WITH COCAINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Chronic substance use related adaptations down-regulate GABAergic transmission (Biggio et al., 2007) and levels of neuroactive steroids (Purdy et al., 1991), which are potent modulators of the GABAA receptor. Physiological adaptations such as blunted heart rate responses to stress provocation are often seen with chronic cocaine use (Sinha et al., 2008), which combined with changes in stress biology contribute to high stress-induced craving and risk of relapse (Milivojevic and Sinha, 2018). Therefore, interventions that potentiate neurosteroids and thereby normalize cocaine use-related adaptations in the autonomic stress response may improve treatment outcomes in cocaine use disorder (CUD). We tested the effects of two doses of the neuroactive steroid precursor pregnenolone (PREG) on experimentally provoked autonomic response in treatment seeking individuals with CUD.
Methods: Thirteen treatment-seeking individuals with CUD were randomly assigned to receive either placebo (PLA; n=4), 300mg PREG/day (n=4) or 500mg PREG/day (n=5). In week 2, they were exposed to three 5-minute personalized guided imagery conditions (stress, cocaine cue, neutral/relaxing), on three separate days in a random, counterbalanced order. Heart rate (HR), Systolic (SBP) and Diastolic Blood Pressure (DBP) were assessed at baseline, immediately following imagery exposure and at regular recovery time points.
Results: A treatment x condition interaction showed that individuals receiving 500mg PREG had significantly decreased HR in stress relative to neutral condition response, compared to individuals receiving 300mg PREG or PLA who had significant stress-induced HR increases. Similarly, SBP increased in response to stress and cocaine cue relative to neutral in the PLA and 300mg PREG groups, but not in the 500mg PREG group. Lastly, DBP increased significantly in stress relative to neutral condition in the PLA group, while it decreased significantly in the 500mg PREG group.
Conclusions: Findings highlight dose-specific effects of PREG on autonomic response in individuals with CUD.
Financial Support: K01DA046561 (Milivojevic), R01AA026514 (Sinha).

CHILDHOOD AND ADULTHOOD TRAUMA IN PERSONS WITH COCAINE DEPENDENCE DIAGNOSIS: EXAMINATION OF SCORES FROM A MODIFIED TRAUMA HISTORY SCREEN

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research

Aim: This study examined trauma exposure scores of volunteers with cocaine dependence (CD; by DSM-IV criteria) compared to normal volunteers (NV). The researchers hypothesized that volunteers with CD have greater exposure to traumatic events than NVs, especially in childhood.
Methods: Male and female adult volunteers from the New York City metropolitan area (n=52 total; n=24 CD and n=28 NV; mean ages 56.2 and 47.8, respectively) were sequentially interviewed by nurse practitioners (February 2019 to November 2021). Volunteers provided informed consent, approved by the Rockefeller University Hospital IRB. Diagnoses were based on the SCID-I interview (DSM-IV criteria). Drug and alcohol exposure were quantified with dimensional measures (KMSK scales). Trauma exposure was scored using a modification of the Trauma History Screen (Carlson et al., 2011; Psychological Assessment 23:463-477).
Results: Volunteers with CD had greater total trauma scores than NV (Mann-Whitney U = 214, p=0.024). However, when adulthood and childhood trauma scores were analyzed separately, there were no significant differences in trauma scores between the two groups. There was also a positive correlation between childhood and adulthood trauma scores for NV (Spearman r = 0.49, p = 0.008); however, no such correlation was observed in persons with CD (Spearman r = 0.089; not significant).
Conclusions: In this exploratory study, volunteers with CD reported greater exposure to traumatic events over their lifespan, compared to NV. However, this was not based specifically in childhood or adulthood trauma. Future studies with larger samples are needed to elucidate these initial findings.
Financial Support: NIH CTSA UL1TR001866; Dr. Miriam and Sheldon G. Adelson Medical Research Foundation

SUBTYPES IN INDIVIDUALS WITH CURRENT COCAINE USE DISORDER AND THEIR IMPAIRMENTS IN NEGATIVE EMOTIONALITY AND EXECUTIVE FUNCTION

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Drug addiction has been linked to impairments in three broad functional domains: 1) approach-related behavior, 2) negative emotionality, and 3) executive function. In our previous work, we described the existence of three distinct neurobehavioral subtypes in those with past substance use disorder, each separately impaired on one of these three domains. Here, we investigated whether similar subtypes exist in a separate sample of participants with current cocaine use disorder (CUD).
Methods: Phenotypic data on function in all three domains was retrieved from the SUDMEX CONN dataset, a Mexican open dataset of CUD patients and matched healthy controls (N = 137, 15% Female). We included all subscales that differed significantly between healthy controls and participants with CUD ($p<0.05$). We determined subtypes within those with CUD (N = 61, 13% Female) by clustering via latent profile analysis on standardized scores.
Results: The best-fit model revealed three subtypes among those with CUD (BIC = -3268.95). These were a 1) 'Low Functioning' type (N=15), with low working memory and high non-planning impulsivity, 2) 'Negative Affect' type (N=22), with elevated general psychiatric symptoms (i.e., anxiety, depression, aggression) and 3) 'Healthy' type (N=24) with minimal impairments. We hence replicated two of the previously found subtypes in this independent sample of patients with current CUD.
Conclusions: These findings provide support for the presence of distinct subtypes in individuals with current CUD, providing further evidence for the need of a personalized medicine approach in addiction. Next steps will include characterizing the neural correlates of the recovered subtypes using the SUDMEX CONN dataset.
Financial Support: A.Z.: NIDA P30 DA048742-01A1, G.D.: NIDA 5T32DA007234-29, D. A-V. and E. A. G-V.: CONACYT-FOSISS project No. 0201493, and CONACYT-Cátedras project No. 2358948

ORAL COMMUNICATION: NEUROSCIENCE OF SUDS II

IN VIVO PHARMACOLOGY OF DIFFERENT DREADD LIGANDS ON LOCOMOTOR ACTIVITY IN RATS

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Drug Category Other, DREADD Ligands
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) are engineered receptors that can be encoded in viral vectors, expressed in specific cell targets, and activated by selective agonists such as clozapine N-oxide (CNO). Target cells expressing DREADDs can then be bidirectionally stimulated or inhibited with these agonists depending on the receptor type and its associated biochemical signaling events. Despite the increasingly pervasive use of chemogenetic tools in preclinical neuroscience research, the in vivo pharmacology of DREADD agonists remains poorly understood. Specifically, there are gaps in our fundamental pharmacological knowledge regarding relative potency, time course and effectiveness of different DREADD agonists. The goal of the current study was to characterize the potency and time course of CNO, Compound 21 (C21), and deschloroclozapine (DCZ) in transgenic Tyrosine Hydroxylase (TH):Cre rats before and after intra-VTA hM3Dq excitatory DREADD injection.
Methods: Ten adult TH:Cre Sprague-Dawley rats (5 female, 5 male) served as subjects. Locomotor activity was monitored for two hours following d-amphetamine (vehicle, 0.1-3.2 mg/kg, IP; positive control), DCZ (vehicle, 0.32-320 µg/kg, IP), CNO (vehicle, 0.32-10 mg/kg, IP), and C21 (vehicle, 0.1-3.2 mg/kg, IP) administration. Behavioral sessions were conducted twice a week prior to and starting three weeks after bilateral intra-VTA hM3Dq DREADD virus injection. Brain tissue was collected after experiment completion for immunohistochemical verification of DREADD expression in TH-positive cells.
Results: d-Amphetamine (0.32-3.2 mg/kg, IP) significantly increased locomotor activity both before and after stimulatory DREADD virus injection. DCZ, CNO, and C21 did not significantly alter locomotor activity pre-DREADD virus injection. DCZ significantly increased activity following DREADD virus injection. CNO and C21 activity studies are ongoing.
Conclusions: Results support the utility of locomotor activity for determining the in vivo potency and time course of different DREADD ligands. Preliminary results suggest that DCZ was less effective than d-amphetamine.
Financial Support: P30DA033934 and T32DA007027

KETAMINE EVOKES SUSTAINED EFFECTS ON BRAIN-DERIVED NEUROTROPHIC FACTOR IN THE CORTICOACCUMBENS CIRCUIT

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Drug Category Sedative/Hypnotics
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Neuropsychiatric disorders classified as synaptopathies (i.e., diseases associated with synaptic dysfunction) are characterized by persistent glutamatergic dysfunction within the corticoaccumbens circuit that affects higher order executive function (e.g., decision making, cognition). This glutamate-associated hypofrontality is marked by a loss of dendritic branching and lack of neurotrophic support. Excitingly, subanesthetic doses of ketamine, known for persistent antidepressant efficacy, increases dendritic branching and immediate release of neurotrophic factors, e.g. brain-derived neurotrophic factor (BDNF). The BDNF gene contains nine different coding sequences. BDNF exon II primarily localizes to dendrites suggesting that alterations in its levels may trigger morphological changes leading to increased synaptic strength in the corticoaccumbens circuit. We tested the hypothesis that repeated, but not single, administration of subanesthetic ketamine increases levels of BDNF exon II mRNA in the prefrontal cortex (PFC) and nucleus accumbens (NAc) 24 hrs following drug administration.
Methods: Male, Sprague-Dawley rats received an intraperitoneal (i.p.) injection of saline, single ketamine (10 mg/kg; 1x/day), or repeated ketamine (10 mg/kg; 1x/day for three days). The PFC and NAc were harvested 24 hrs following the dosing regimen; mRNA was extracted and converted to cDNA. Levels of BDNF exon II mRNA were quantified using reverse transcriptase polymerase chain reaction (RT-PCR);

cyclophilin A (PPIA) was used as a loading control. Gene expression differences in ketamine-treated rats were identified versus saline-treated rats.
Results: Repeated, but not single, ketamine administration increased NAc BDNF exon II mRNA levels versus saline ($p<0.05$). Data analyses for the effects of ketamine on BDNF exon II mRNA levels in the PFC are ongoing.
Conclusions: Dosing regimen-dependent, long-term effects of ketamine administration on BDNF mRNA levels are detectable in the rodent brain. Taken together, ketamine-mediated BDNF exon II mRNA levels may sustain synaptic strengthening mechanisms supporting future investigation into the utility of ketamine for diseases characterized by synaptopathies.
Financial Support: R00 DA033374 and UTMB Center for Addiction Research

MGLU1 ACTIVATION REVERSES PERSISTENT DEFICITS IN PREFRONTAL CORTEX INHIBITORY TRANSMISSION AND WORKING MEMORY INDUCED BY ADOLESCENT COCAINE EXPOSURE

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Exposure to psychostimulants, such as cocaine, during adolescence produces persistent changes in the PFC which parallel cognitive deficits seen in adulthood. Further, adolescent exposure to psychostimulants impairs inhibitory transmission in the PFC in adulthood, suggesting that enhancing PFC inhibitory transmission may be a promising strategy to reverse drug-induced cognitive deficits. Activation of the mGlu1 subtype of metabotropic glutamate receptor increases inhibitory transmission in the PFC and working memory by selective excitation of somatostatin-expressing GABA interneurons (SST-INs). Therefore, we hypothesize that repeated exposure to cocaine during a critical developmental period in adolescence disrupts PFC inhibition via SST-INs and drives working memory impairments in adulthood which can be mitigated by activation of mGlu1.
Methods: Approach: mGlu1 PAMs, SST- and PV-Ai9 tdTomato mice, whole-cell patch-clamp electrophysiology, maze- and touchscreen-based automated cognition testing.
Model: Male and female mice were injected once daily with 20mpk cocaine for 7 days (PND 35-42). Behavioral and electrophysiological testing was conducted between 10-12 weeks of age.
Results: We found that repeated administration of cocaine during a critical adolescent period impaired PFC SST-IN, but not parvalbumin-expressing interneuron (PV-IN), firing compared to saline-treated mice. Adolescent cocaine exposure significantly decreased the frequency of spontaneous excitatory postsynaptic currents onto SST-INs but not PV-INs. These findings were paralleled by adolescent cocaine-induced impairments in spatial working memory in adulthood. Importantly, these physiological and behavioral effects of adolescent cocaine exposure were reversed by selective mGlu1 activation. Lastly, repeated amphetamine administration during the same adolescent critical period did not result in impaired SST-IN function or spatial working memory in adulthood.
Conclusions: These studies show that: 1) cocaine, but not amphetamine, exposure during an adolescent critical period induces persistent and selective deficits in PFC SST-IN function and cognition in adulthood and 2) selective activation of mGlu1 with PAMs represents a novel strategy for reversing cocaine-induced cognitive impairments.
Financial Support: MH119673, NS031373, MH062646, MH073676, MH065215

EXTRACELLULAR MATRIX AND CLOCK MOLECULE ABNORMALITIES IN SUBJECTS WITH COMORBID SUBSTANCE USE DISORDER AND MAJOR DEPRESSION

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Neurobiology/Neuroscience

Abstract Detail Human
Abstract Category Original Research
Aim: Substance use disorders (SUD) are a debilitating family of psychiatric disorders that share comorbidity with major depressive disorder (MDD), making it challenging to identify neurobiological factors underlying SUD or MDD. We used a cohort of subjects with comorbid SUD and MDD and subjects with MDD or SUD only to examine neuropathological alterations. Evidence points to altered expression of extracellular matrix (ECM) and clock molecules in SUD. Chondroitin sulfate proteoglycans (CSPGs) are ECM molecules that form perineuronal nets (PNN) around inhibitory neurons. Rodent models suggest that PNNs are degraded by endogenous proteases to allow for formation of reward memories and then reconsolidate to protect these memories. Recent work from our group and others reported circadian modulation of PNN composition. Furthermore, sleep and circadian rhythm disturbances are common in SUD and MDD. We tested the hypothesis that ECM and clock molecules are differentially altered in subjects with SUD vs MDD.
Methods: We used hippocampal samples from donors with SUD (n=20), SUD and MDD (SUD/MDD, n=24), MDD only (MDD, n=20) and controls (n=20). CSPGs were labeled with Wisteria floribunda agglutinin lectin and quantified using stereology-based software. Gene expression was determined using QRT-PCR. Stepwise linear regression analysis of covariance was used to test for effects of diagnosis group and confounding variables.
Results: We observed a gradient of PNN and CSPG-glial cell changes from SUD to MDD. PNN densities were increased in SUD, compared to moderate changes in SUD/MDD and decreased PNNs and increased CPSG-glia in MDD. Similar gradients were observed for ECM and clock molecules.
Conclusions: Our findings point to differential ECM and clock molecule neuropathology between SUD and MDD. Lack of changes in subjects with comorbid SUD and MDD point to the need to study these groups both together and independently and suggest substance use may in part compensate for alterations in ECM molecules in MDD.
Financial Support: 1R01MH125833 and GM103328

ORAL COMMUNICATION: FENTANYL: FOCUS ON TOXICOLOGY

PHARMACOLOGICAL CHARACTERIZATION OF NON-FENTANYL SYNTHETIC OPIOIDS THAT ARE APPEARING IN CLANDESTINE DRUG MARKETS

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[1]NIDA, Intramural Research Program
Drug Category Opiates/Opioids
Topic Mechanisms of Action
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Illicitly manufactured fentanyl is driving the current opioid crisis, but a number of non-fentanyl synthetic opioids have emerged on clandestine drug markets worldwide. Little information is available about the pharmacology of most novel opioids when they first appear on the market. U-47700, brorphine, and isotonitazene are examples of non-fentanyl synthetic opioids associated with human overdose fatalities.
Methods: Here, we investigated the pharmacology of U-47700, brorphine, and isotonitazene using in vitro and in vivo methods. In vitro receptor bindings assays were carried out in rat brain membranes using [3H]DAMGO, [3H]DADLE, or [3H]U-69593 to label mu-, delta-, or kappa-opioid receptors, respectively. In vivo experiments were carried out in male Sprague-Dawley rats to examine the effects of s.c. drug administration on hot plate antinociception, catalepsy scores, and body temperature. Ki affinity values and ED50 potency values were determined by nonlinear regression analyses.
Results: The non-fentanyl opioids displayed greater affinity for mu- over delta- and kappa-opioid receptors. Ki values at the mu-opioid receptor were 15.4 nM for U-4770, 32.8 nM for brorphine, and 14.9 nM for isotonitazene, and these values were weaker than that of morphine (Ki=5.3 nM)(N=3 experiments per drug). When administered to male rats, all compounds induced dose-dependent antinociception, catalepsy, and hypothermia (N=8 rats for per dose). Findings from the hot plate test revealed that ED50 values for U-47700 (0.404 mg/kg), brorphine (0.086 mg/kg), and isotonitazene (0.007 mg/kg) were much more potent than morphine (4.164 mg/kg s.c.). Isotonitazene was more potent than fentanyl (0.021 mg/kg, s.c.) as an antinociceptive agent.

Conclusions: Our results demonstrate that non-fentanyl synthetic opioids can be much more potent than morphine in vivo, posing serious risks for unsuspecting users. Importantly, the in vitro mu-opioid receptor binding affinity for a given synthetic opioid may not predict its in vivo potency.
Financial Support: NIDA IRP

REINFORCING EFFECTS OF FENTANYL AND FENTANYL ANALOGS FOUND IN ILLICIT DRUG MARKETS

Charles Schindler[*1], Shelby McGriff[1], Eric Thorndike[1], Michael Chojnacki[1], Michael Baumann[1]*
[1]NIDA Intramural Research Program
Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Illicitly manufactured fentanyl and fentanyl analogs are the main drivers of the worsening opioid epidemic. Although the pharmacology of fentanyl is well characterized, there is little information about the reinforcing effects of newly emerging fentanyl analogs that are contributing to opioid overdose. Here, we compare the effects of fentanyl and the clandestine fentanyl analogs, cyclopropylfentanyl and butyrylfentanyl, on drug self-administration behavior in male rats.
Methods: Sprague-Dawley rats fitted with intravenous (i.v.) jugular catheters were placed in experimental chambers containing two nose poke holes. Active nose poke responses resulted in delivery of a constant volume of drug (0.2 mL) over a period of 2 s on a fixed-ratio 1 schedule, followed by a 20 s timeout. Acquisition doses for the compounds were 0.01 mg/kg/inj for fentanyl and cyclopropylfentanyl, 0.03 mg/kg/inj for butyrylfentanyl, while 0.1 mg/kg/inj was used for heroin. Following 10 days of acquisition training, dose-effect testing began with three additional doses, each of which were tested for 3 days. Subjects then returned to the original training dose until responses stabilized and underwent saline extinction.
Results: Acquisition of fentanyl self-administration was achieved by male rats, with significant differences between active versus inactive nose pokes over the last 4 days of training ($p<0.05$). A similar profile of acquisition was seen for heroin and cyclopropylfentanyl. Both fentanyl and cyclopropylfentanyl showed a typical inverted-U dose-effect function during dose-effect testing. Maximal response rates were similar among all drugs, with fentanyl showing maximum responding at 0.001 mg/kg/inj, cyclopropylfentanyl at 0.003 mg/kg/inj, and heroin at 0.003 mg/kg/inj. Preliminary data for butyrylfentanyl suggests a similar self-administration profile.
Conclusions: Comparison between heroin, fentanyl, cyclopropylfentanyl and butyrylfentanyl show that these compounds support self-administration, indicating that emerging fentanyl analogs display significant abuse liability and may contribute to compulsive use in humans.
Financial Support: Supported by the Intramural Research Program of NIDA/NIH (Z01DA000523)

A SECONDARY ANALYSIS EXAMINING FENTANYL'S IMPACT ON OPIOID WITHDRAWAL SYMPTOMS AND EXPLORING THE ROLE OF BODY WEIGHT IN FENTANYL CLEARANCE

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Fentanyl, a lipophilic opioid contributing to increased drug overdose and complicating treatment of opioid use disorder (OUD), may result in more severe withdrawal symptoms than heroin. Little is known about fentanyl dependence or metabolism.
Methods: This secondary analysis, from a 14-day inpatient study on the safety and efficacy of sublingual dexmedetomidine for opioid withdrawal, includes participants with OUD who were maintained on morphine (30mg QID) for five days before starting study medication. Urine toxicology and opioid withdrawal (COWS and SOWS) were assessed daily.

Results: Participants (n=135) had a mean age of 42.02 (SD = 10.95). 120 participants (88%) tested positive for fentanyl on admission and continued to test positive for 7.17 days on average (SD= 2.75; range 2-14). We compared withdrawal symptoms between participants positive for fentanyl (FP) at admission (n=120) and those fentanyl-negative (FN) (n=15) using Welch's t-tests. FP participants had significantly higher mean ($p < 0.01$) and maximum ($p < 0.05$) COWS scores on days 1-3 and significantly higher mean ($p < 0.001$) and maximum ($p < 0.01$) SOWS scores on day 1.
We compared fentanyl clearance and withdrawal between those who were overweight or obese (OO; n=72) and those with a healthy BMI (HB; n=63). OO participants consistently had a higher proportion of FP urine samples. Chi-square tests confirmed significant differences on days 7 ($p< 0.05$), 8 ($p < 0.01$), and 10 ($p< 0.05$). OO participants had significantly higher SOWS scores on days 4 and 5 ($p < 0.05$).
Conclusions: Fentanyl withdrawal was objectively (COWS) more severe than heroin withdrawal on days 1-3 and subjectively (SOWS) more severe on day 1. OO individuals demonstrated a significantly higher proportion of FP urine samples, and higher subjective withdrawal compared to HB participants. Further work on fentanyl metabolism and clearance, fentanyl withdrawal symptoms, and whether BMI influences these outcomes is needed.
Financial Support: BioXcel Therapeutics Inc.

LOW INCIDENCE OF PRECIPITATED WITHDRAWAL IN ED-INITIATED BUPRENORPHINE, DESPITE HIGH PREVALENCE OF FENTANYL USE

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Anecdotal and limited reports cite concerns regarding precipitated withdrawal (PW) with standard buprenorphine (BUP) induction among fentanyl users. We sought to determine the incidence of PW in trial of ED-initiated BUP.
Methods: We report data from an ongoing trial, ED INNOVATION from 7/12/20-12/10/21 in 28 diverse U.S. emergency departments (ED). Patients >18 with untreated OUD, Clinical Opiate Withdrawal Scale (COWS) score of > 4 and urine negative for methadone are randomized to sublingual (SL-BUP) or 7-day extended-release injectable (XR-BUP) induction. SL-BUP patients receive instructions for unobserved BUP initiation if COWs (4-7) or 8-12 mg SL-BUP administered in the ED if COWS > 8; XR-BUP is administered for COWS > 4. Patients receiving any ED BUP are observed for 2 hours. Possible PW events are reviewed by an expert panel.
Results: Among 800 enrolled, 67% were male; 58% White, 30% Black. Urines were positive for fentanyl (76%), multiple drugs(82%), cocaine(34%), marijuana(46%) and opiates(45%). 16% had COWS 4-7. Ten patients (1%) experienced PW; 6 in SL-BUP group and 4 in XR-BUP. Of those with PW: 70% were male; mean age 40 years; 30% White, 60% Black, 10% American Indian. Most (80%) urines revealed multiple drugs; fentanyl(100%), cocaine(50%), marijuana(30%) and opiates(30%). Among those with PW, mean baseline COWS score was 16(range 8-29). Patients presented in different stages of withdrawal: 3 mild (COWS of 8-12); 6 moderate (13-24); and 1 severe (29). The average number of hours since last opioid use was 16 hours (range 8-24). All cases of PW improved with protocol-driven treatment and discharged; 2 were observe overnight in ED.
Conclusions: Only 1% of patients initiated on BUP in 28 U.S. EDs experienced PW, despite high prevalence of fentanyl use. Patients who use fentanyl may be less likely to experience PW than the anecdotal reports. PW can be effectively treated.
Financial Support: This research was supported by the National Institutes of Health through the NIH HEAL Initiatives under award number 3UG1DA015831-18S7

ORAL COMMUNICATION: CRAVINGS AND CUES IN SUDS

CENTRALITY OF CRAVING IN NETWORK ANALYSIS OF DSM-5 SUD DIAGNOSTIC CRITERIA FOR ALCOHOL, CANNABIS, TOBACCO, OPIOIDS, AND COCAINE

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Drug Category Other, Alcohol, Cannabis, Tobacco, Opioids, and Cocaine
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Among the 11 DSM-5 substance use disorders (SUD) diagnostic criteria, craving is a potential central marker for understanding mechanisms and for treatment. Recent research proposes that diagnostic criteria are dynamically directly related to each other. Symptom network analysis explore these interrelationships, considering that they are causally mutually dependent, and influence each other accordingly in these networks.
Our objective was to explore craving centrality across substance use disorders based on the study of symptom interactions in cross-sectional network analyses of DSM-5 SUD diagnostic criteria.
Methods: Participants were recruited from outpatient addiction clinics in Aquitaine, France. Analyzes were conducted among regular users (2 times per week threshold) with at least one DSM-5 SUD (n = 1,359) for alcohol, cocaine, tobacco, opioids, or cannabis. Original Investigation with a decision analytical model was conducted on the 11 DSM-5 SUD criteria evaluated over the past 12 months and collected at treatment intake.
Results: The only symptom that consistently remained in the top five most influential measures in terms of centrality was craving, indicating that it exhibited a high degree of connections in the entire symptom network regardless of the substance. No centrality indices were outside the estimation of the confidence intervals on the edge weights, with a CS-coefficient for strength near to zero for Opiate and Cocaine (the two addictions with a limited number of subjects, respectively N = 131 and N = 141), at 0.67 for Alcohol, 0.59 for Tobacco, 0.44 for Cannabis and at 0.52 for all addictions.
Conclusions: These important results suggest that Craving could be a core marker for the onset and chronicity of SUD and confirms its interest as a major target for treatment across addictions. Furthermore, the lack of differences between the networks across substances supports the existence of a general construct at the origin of the different SUDs.

THE ROLE OF EMOTION DYSREGULATION IN THE RELATIONSHIP BETWEEN ANHEDONIA AND OPIOID CRAVING

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid-related overdose is the leading cause of death among people being released from incarceration. Opioid craving can increase risk for relapse, but research on factors that predict opioid craving is lacking. Anhedonia (i.e., failure to experience pleasure) has been identified as a likely predictor of opioid craving, and this may be intensified by poor regulation of emotions, however, these relationships have yet to be examined among people involved in the justice system. This study investigated whether anhedonia was positively associated with opioid cravings, and whether emotion dysregulation strengthened this relationship in a justice-involved sample.
Methods: Participants were adult men and women receiving court-mandated substance use treatment after incarceration (n = 167). Participants completed measures of their demographics, anhedonia, opioid cravings, emotion dysregulation, and other substance use. Moderation models were used to test whether anhedonia predicted opioid cravings and whether this relationship was moderated by overall/subscales of emotion dysregulation. Other substance use was controlled for.

Results: Anhedonia and opioid cravings were significantly related at the bivariate level (r = .32, p=.003). Overall emotion dysregulation (b=.09, t(85)=2.54, p=.01) and difficulties controlling behaviors when distressed subscale (b=.45, t(85)=3.30, p=.002) had a significant, positive effect on cravings in multivariate models. There was no evidence of moderation by emotion dysregulation. However, post-hoc analyses with a subsample of people who used heroin frequently (n = 57) indicated an interaction wherein the relationship between anhedonia and opioid cravings was strong and positive at high levels of difficulty controlling behaviors when distressed, but nonsignificant at low levels, F(1, 49)=5.51, p=.02.
Conclusions: Emotion dysregulation may increase opioid cravings among justice-involved people. Facets of emotion dysregulation may also intensify the impact of anhedonia on opioid cravings among justice-involved individuals with severe heroin use.

ROLE OF VENTRAL SUBICULUM NEURONAL ENSEMBLES IN INCUBATION OF OXYCODONE CRAVING AFTER ELECTRIC BARRIER-INDUCED VOLUNTARY ABSTINENCE

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: To study relapse to oxycodone seeking after electric barrier-induced voluntary abstinence
Methods: We trained Sprague-Dawley or Fos-lacZ transgenic male and female rats to self-administer oxycodone (0.1 mg/kg/infusion, 6-h/d) for 14 days. The rats were then exposed for 14 days to an electric barrier of increasing intensity (0.1 to 0.4 mA) near the drug-paired lever that caused voluntary abstinence or were exposed to 14 days of forced abstinence. We tested Sprague-Dawley rats for relapse to oxycodone seeking without shock and drug on abstinence day 15 and extracted their brains for Fos-immunohistochemistry, or tested them after vSub vehicle or muscimol-baclofen injections on abstinence days 1 and 15. We performed Daun02 inactivation of relapse-activated vSub Fos neurons in Fos-lacZ transgenic rats on abstinence day 15 and then tested them for relapse on abstinence day 18.
Results: Relapse after electric barrier-induced abstinence increased Fos expression in vSub. Muscimol-baclofen inactivation or Daun02 selective inactivation of vSub Fos-expressing neuronal ensembles decreased “incubated” oxycodone seeking after voluntary abstinence. Muscimol-baclofen vSub inactivation had no effect on non-incubated opioid seeking on abstinence day 1 or incubation after forced abstinence.
Conclusions: Results demonstrate a selective role of vSub neuronal ensembles in incubation of opioid craving after cessation of drug self-administration by adverse consequences of drug seeking.
Financial Support: NIDA

ACTION-TENDENCY RETRAINING IN SEVERE PSYCHIATRIC INPATIENTS WITH STIMULANT USE DISORDER: A PRELIMINARY ANALYSIS ON STIMULANT CRAVING AND TREATMENT OUTCOMES

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Behavioral treatments for stimulant use disorders, relying on top-down cognitive processes, have thus far yielded only modest outcomes. Implicit-learning approaches, such as action-tendency retraining, have been shown to reduce relapse in other substance use disorders. Here, we present preliminary data on stimulant craving following action-tendency retraining in severe psychiatric inpatients with primary stimulant use disorders.
Methods: 47 inpatients were randomized to 14 sessions of active treatment (N=21; 40.2±12.2 years old, 7F) or control sham-training (N=27; 41.3±10.9 years old, 10F) across 8 weeks. Sessions comprised a 20-minute

implicit training task: pushing/pulling a joystick in response to non-drug- and drug-related images. Active treatment participants were prompted to push on all drug-related images, whereas controls equally pushed/pulled across stimuli type. Subjective stimulant craving was assessed at baseline, 4-, 8- and 12-weeks. Demographics and diagnostic status were retrieved via patient charts. Because data collection is ongoing, treatment outcome data will be reported with the full presentation.
Results: Most prevalent diagnoses were 65% psychosis, 40% mood, and 30% stress-related disorders, with 90% having ≥2 substance use disorders. Groups were similar in demographics, diagnoses, and primary stimulant of use (methamphetamine, cocaine). There was a pattern for overall lower stimulant craving reported by active treatment participants than controls, but this difference was not statistically significant (p=.07; BF01=.54). Stimulant craving across the sample was not associated with diagnoses, stimulant use patterns before treatment, and time between treatment admission to study enrollment (BF01 ranged 1.42-.5.4).
Conclusions: We found some preliminary evidence to suggest action-tendency retraining reduces stimulant craving in patients with primary cocaine or methamphetamine use disorders. This is the first study to investigate the viability and clinical utility of action-tendency retraining targeting stimulant use in a psychiatric population with severe complex concurrent disorders. Analyses with full data are planned to assess the effects of training on treatment outcome.
Financial Support: Funding support for this project was provided by BC Mental Health and Substance Use Services Research Institute, the BC Children's Hospital Research Institute, and the Child and Family Research Institute

ORAL COMMUNICATION: FENTANYL:FOCUS ON SUBJECTIVE/AFFECTIVE PROPERTIES

CHARACTERISTICS AND CORRELATES OF FENTANYL PREFERENCES AMONG PEOPLE WITH OPIOID USE DISORDER (OUD)

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Fentanyl has come to dominate the U.S. illicit opioid supply. We aim to characterize and examine correlates of preferences for fentanyl vs. other opioids among individuals starting OUD treatment.
Methods: We interviewed 250 adults initiating buprenorphine treatment who had a fentanyl-positive urine test at intake. We examined bivariate associations between people who prefer fentanyl (PPF) and sociodemographic characteristics, psychosocial factors, substance use patterns, overdose experiences, opinions about treatment, and harm reduction behaviors. We then used logistic regression to examine independent associations with fentanyl preferences.
Results: Over half (52.0%) of participants preferred fentanyl over other opioids (21.2% fentanyl alone, 30.8% heroin-fentanyl mix). Compared to heroin, PPF reported fentanyl had faster onset (76.7%), longer lasting effects (50.9%), and stronger (97.4%) and better high (71.6%). PPF were willing to pay more (61.5%) and look longer (70.8%) for fentanyl-containing opioids. Compared to people preferring non-fentanyl opioids, PPF were younger (mean 39.7 vs. 46.4 years; P<0.001) and more likely to be White (38.5% vs. 25.8%; P=0.033) and to have administered naloxone to someone (60.0% vs. 46.7%; P=0.035). In the past 30 days, compared to people preferring non-fentanyl opioids, PPF experienced greater psychological distress (mean score 19.4 vs. 17.4; P=0.005), spent more money on drugs (median $2,000 vs. $1,326; P=0.009), and reported more days of income-generating crime (mean 14.6 vs. 9.0 days; P=0.001), cocaine use (mean 15.6 vs. 11.0 days; P=0.004), and polysubstance use (mean 19.6 vs. 16.1 days; P=0.021), but fewer days of non-prescribed buprenorphine use (mean 0.87 vs. 2.1 days; P=0.028). Variables independently associated with PPF status in the regression model included age (OR: 0.949; P<0.001) and non-prescribed buprenorphine use (OR: 0.912; P=0.018).
Conclusions: Many people with OUD report preferring fentanyl, and PPF differ substantively from those with other opioid preferences. Understanding preferences surrounding fentanyl could inform treatment and harm reduction interventions.

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HIGH RATES OF FENTANYL IN NON-OPIOIDS REPORTED WITH FENTANYL TEST STRIP USE IN PHILADELPHIA, PA

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Fentanyl test strips (FTSs) are a promising harm reduction strategy to reduce the risk of overdose among people who use drugs that may be contaminated with fentanyl. The prevalence of fentanyl in non-heroin drugs is unknown. The aim of this study was to determine the presence of fentanyl in non-heroin drugs as detected by people who use drugs' (PWUD) use of FTS and behavioral outcomes after testing.
Methods: A survey of PWUD conducted between January-May 2021 in Philadelphia, PA outside a harm reduction organization. PWUD were asked about their last FTS use on a non-heroin drug and univariate statistics were generated using SPSS.
Results: Among 86 participants, 70.9% (n=61) reported a positive result during last FTS use on a non-opioid, most commonly in methamphetamine, synthetic cannabinoids, and cocaine. Among those who reported a positive FTS result, 26.2% (n=16) reported actions to reduce risk of an opioid overdose such as not using the drug or altering use. The majority of participants were White (67%) and male (72%) and had an average age of 39.6 years.
Conclusions: Among our sample, fentanyl was reported in the majority of non-heroin drugs. If accurate, consumption of any illicit non-opioid drug in Philadelphia is placing people at high risk of unintentional fentanyl overdose. There is a critical need for research to determine testing accuracy, accuracy of interpretation of test results, and the true prevalence of fentanyl in the non-heroin market in Philadelphia.
Financial Support: This work was supported by Vital Strategies through funding from Bloomberg Philanthropies.

FENTANYL SAFETY STRATEGIES AND TRENDS: A MIXED-METHODS EXPLORATION USING REDDIT

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Drug Category Other, Multi drug/fentanyl contamination
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: The current study utilized the anonymous user-generated content on the social media site Reddit to (1) examine the protective strategies employed by persons who use drugs (PWUD) as related to current fentanyl contamination in opioid and non-opioid drug supply, and (2) explore trends in discussions of fentanyl contamination concerns by drug type over time.
Methods: We used 34 fentanyl search terms, containing analogs and common misspellings, to search 72 drug-related subreddits from 2014 to 2021. To examine current fentanyl protection strategies for the qualitative aim, we examined a random sample of 500 posts in 2021. Posts were first screened for relevance for inclusion (i.e., focus on fentanyl contamination of drug supply). Relevant posts (N=226) were coded using a codebook created a priori. To explore trends in post volume over time for the quantitative aim, we ran linear regressions with relative post volume as a function of time in years, as both linear and quadratic functions.
Results: The majority (60%) of sampled posts expressed fear or anxiety over fentanyl contamination. 41% of posts described suspected fentanyl contamination due to the way a drug looked or how it made the poster feel. The most common protective strategy against using contaminated drugs was use of social networks to warn of contamination (42%). Reagent testing (16%) and trying a smaller sample (11%) were also discussed. Overall, relative post volume did not significantly increase across all subreddits. However,

statistically significant increases were detected for 'over the counter' and 'stimulant' drug subreddits ($p<.05$). Quadratic increases were not significant, except for the 'multiple drug' subreddits ($p<.05$).
Conclusions: The current research found individuals engage in a multitude of protective strategies across a range of substances in the current era of fentanyl contamination. Even still, anxiety around contamination was common, and trends indicate increase in discussions among non-opioid drug subreddits.
Financial Support: Supported by 1K01DA053435, 5K01DA046697, and 5R25DA037190.

STRATEGIES USED TO AVOID FENTANYL EXPOSURE AND FATAL OVERDOSE AMONG RURAL PEOPLE WHO USE DRUGS: MULTI-SITE QUALITATIVE FINDINGS FROM THE RURAL OPIOID INITIATIVE

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Illicitly manufactured fentanyl is now the primary driver of opioid overdose deaths in the United States (US). People who use drugs (PWUD) may become exposed to fentanyl either intentionally or unintentionally when their illicitly obtained drugs contain or are adulterated with fentanyl without their knowledge. This study sought to identify strategies used to prevent fentanyl exposure and fatal overdose.
Methods: Semi-structured qualitative interview data from the Rural Opioid Initiative (ROI) was used for this analysis. The analysis consists of 298 semi-structured qualitative interviews across 9 states and 58 counties. The qualitative interview guides were harmonized, and preliminary coding labeled emergent themes in accordance with the interview questions. After preliminary codes were applied all data with a label of fentanyl were re-coded in-vivo, focusing on the words used by participants. We then queried the larger data set for the terms discovered in-vivo to capture all fentanyl mentions regardless of interview questions.
Results: Most participants reported an awareness and concern that fentanyl had saturated the drug market, regardless of their drug of choice. Strategies used to prevent fentanyl exposure were: 1) avoidance, 2) buying drugs from trusted sources, 3) using fentanyl test strips, 4) using small doses (i.e., "tester" shots) and/or non-injection routes, 5) using with other people, 6) tasting, smelling, and looking at drugs before use, and 7) carrying and using naloxone to reverse overdoses. Most PWUD used a combination of these strategies as there was an overwhelming fear of fatal overdose.
Conclusions: PWUD living in rural areas of the US are aware that fentanyl is in their drug supply and used several strategies to prevent fatal overdose. Increasing access to harm reduction services, such as fentanyl test strips, naloxone, drug testing, and safe consumption sites should be prioritized to address the current overdose crisis.
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ORAL COMMUNICATION: TOWARDS STANDARDIZATION OF CLINICAL TRIAL OUTCOMES

VALIDITY OF THE DSM-5 TOBACCO USE DISORDER DIAGNOSTICS IN ADULTS WITH PROBLEMATIC SUBSTANCE USE

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Drug Category Nicotine/Tobacco
Topic Substance Use Disorder

Abstract Detail Human
Abstract Category Original Research
Aim: DSM-5 tobacco use disorder (TUD) nosology differs from DSM-IV nicotine dependence (ND) by including abuse and craving criteria, utilizing a lower threshold (≥2 criteria), and defining severity levels (mild; moderate; severe). We examined the concurrent and prospective validity of DSM-5 TUD and TUD severity and whether DSM-5 TUD diagnosis showed greater validity than DSM-IV ND diagnosis.
Methods: Data were analyzed on respondents with past year smoking (N=396) from a convenience sample of U.S. adults with current problematic substance use. The baseline assessment collected information on DSM-IV ND and DSM-5 TUD criteria, smoking-related variables, and psychopathology. Electronic daily assessments queried smoking and cigarette craving for the following 90 days. Using variables expected to be related to TUD (validators), e.g., cigarette consumption, cigarette craving scale, Fagerström Test for Nicotine Dependence, and other psychiatric disorders, regression models estimated the association of each baseline (concurrent) and prospective validator with DSM-5 TUD and DSM-5 TUD severity levels and whether association differed for DSM-5 TUD and DSM-IV ND diagnoses.
Results: Both DSM-5 TUD and DSM-IV ND were associated with most concurrent validators (p-values<0.05), with significantly stronger associations with DSM-5 TUD for number of days smoked (p=.0231) and smoking craving scale (p=.0067). Baseline DSM-5 TUD and DSM-IV ND predicted prospective smoking and craving on any given day during follow-up, with stronger associations for DSM-5 TUD (association difference [95% CI]: any smoking, 0.53 [0.27, 0.77]; number of cigarettes smoked, 1.36 [0.89, 1.78]; craving scale, 0.19 [0.09, 0.28]). All validators were associated with severe TUD, most were associated with moderate TUD, and some were associated with mild TUD.
Conclusions: The DSM-5 TUD diagnostic measures as operationalized in this study demonstrated concurrent and prospective validity. Inclusion of new criteria improved validity and clinical relevance, perhaps because craving plays a key role in development and maintenance of TUD through impaired control over use.
Financial Support: NIH grants R01DA018652 and 1R01AA025309; New York State Psychiatric Institute.

QUANTIFYING THC CONSUMED BASED ON SELF-REPORT OF CANNABIS PRODUCT, ADMINISTRATION METHOD, QUANTITY AND FREQUENCY OF USE

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Drug Category Cannabis/Cannabinoids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: With increasing legalization and prevalence of cannabis use, better quantification of delta-9 tetrahydrocannabinol (THC) consumption is needed to more precisely assess the relationship between consumption and various risks. Quantification requires a standard metric that applies to various cannabis products. We explored a method for estimating milligrams of THC (mgTHC) consumed per day, based on self-report of: "hits" (puffs or tokes) taken of a product (flower vs. concentrate), method of administration (smoked vs. vaporized), and use patterns.
Methods: Adult cannabis users completed an online survey assessing demographics, frequency, quantity, method of administration, and potency of past-7-day use. This analysis included a subset (n=889) of participants who smoked or vaped flower or concentrate products and chose to report quantity of use in hits. We estimated the amount of cannabis material consumed per hit using constants derived from lab studies (60mg/hit for flower, 12mg/hit for concentrates). Milligrams of material (# of hits x mg/hit constant) were multiplied by self-reported product potency to yield unadjusted estimates of mgTHC consumed. An adjusted metric of mgTHC was obtained by correcting for loss of THC due to administration efficiency (e.g., side-stream, trapped THC, pyrolysis), using efficiency constants: 0.3 for smoking flower, 0.6 for dabbing concentrates, and 0.5 for vaping flower or concentrates.

Results: The unadjusted estimate of average mgTHC consumed in a typical day from flower (111.2±102.9) was greater than from concentrates (70.1±71.8). The adjusted estimate of mgTHC from flower (34.0±31.8) was similar to that from concentrates (35.4±36.1).
Conclusions: The adjusted model appeared to yield more face-valid estimates and was consistent with the self-titration hypothesis that individuals consume less higher-potency cannabis products. These models provide one method that may be useful for estimating mgTHC at the population level. Further refinement and validation of estimation models are needed to provide more precise and reliable estimates.
Financial Support: Supported by: R01DA050032-01

DEVELOPING STANDARDIZED POTENCY AND QUANTITY SURVEY ITEMS FOR ASSESSING POPULATION-LEVEL CONSUMPTION OF CANNABIS FLOWER AND CONCENTRATE PRODUCTS

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Standardized cannabis consumption measures are needed to accurately determine consumption risk levels in order to develop safety guidelines and inform public policy. Measurement is complicated by cannabis product heterogeneity (e.g., preparations, potencies, administration methods) and uncertainty about which items best measure aspects of consumption among users. We are developing a flexible, personalized survey to measure quantities and patterns of THC consumption using items that participants feel best reflects their use, and piloted response patterns for candidate items.
Methods: Adult cannabis users (n=4,010) completed an online survey permitting participants to report quantity either as "hits per day" or "grams per week". Items assessed past 7-day quantities, potencies (%THC), and frequencies of cannabis flower and concentrate products. Respondents rated their confidence (0-100) in their estimates of potency and grams, and indicated whether their past 7-day pattern was typical.
Results: Hits per day vs. grams per week were reported by 38% and 62%, respectively. Quantity was greater for flower than concentrate products whether reported as hits (median flower=9 hits, IQR: 9 vs. median concentrate=6 hits, IQR: 9) or grams (89% vs. 44% using 1+ grams of flower and concentrates, respectively), supporting item validity. High mean confidence ratings for potency and quantity estimation (range 83-89), and high probabilities of reporting the past week as "typical" (87% and 65% among daily and non-daily consumers, respectively) supported the potential of such items for extrapolating quantity estimates beyond a single week. Responses to the 3-category flower potency item were skewed (74% endorsing highest option of 16-30% THC) suggesting a need to modify response options.
Conclusions: Results from this online sample suggest that a customizable, valid set of cannabis use items can reliably estimate patterns and quantities of THC consumption at a population level.
Financial Support: R01DA050032-01, T32-DA037202, P30-DA037202

PERCENTAGE OF NEGATIVE URINE SPECIMENS AS A CLINICALLY MEANINGFUL ENDPOINT FOR RCTS EVALUATING TREATMENT FOR COCAINE USE

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Drug Category Stimulants
Topic Other
Abstract Detail Human
Abstract Category Original Research
Aim: Recent FDA guidance indicated drug use patterns other than abstinence can be accepted as endpoints in clinical trials, provided there is an association with better health outcomes or psychosocial functioning. Whereas multiple evaluations have examined drug use patterns based on patient self-report, few have

examined non-abstinence patterns based on urine toxicology. This study examined a threshold based on the percentage of cocaine-negative urine specimens collected during treatment as a potential meaningful endpoint. We hypothesized that individuals providing at least 75% cocaine-negative urine specimens would have better long-term outcomes than those providing less than 75% cocaine-negative urines.
Methods: Data were pooled across seven RCTs evaluating behavioral and/or pharmacological cocaine use treatments, resulting in a sample of 760 treatment-seeking individuals (64.3% men, 50.9% Caucasian). Urine specimens were collected at least once per week during the treatment period across all trials. Participants were grouped according to whether they provided at least 75% cocaine-negative urines (>75%-Group; n=126) or not (<75%-Group). Chi-squares and ANOVAs compared demographic and clinical characteristics and within-treatment and follow-up outcomes between the groups.
Results: Regarding baseline characteristics, the >75%-Group had a greater percentage of males and were less likely to be never married/living alone, unemployed, and on public assistance than the <75%-Group. During treatment, compared to the <75%-Group, the >75%-Group had more days retained in treatment (M=66.9, SD=21.9 versus M=49.7, SD=32.6; F(1, 757)=32.22, p<.001), a greater percentage of days abstinent from cocaine (M=96.6, SD=6.5 versus M=67.1, SD=26.2; F(1, 673)=153.62, p<.001), and a greater reduction in cocaine use frequency (M=0.9, SD=0.3 versus M=0.4, SD=0.4; F(1, 587)=107.73, p<.001). At several follow-up assessments (up to 12 months), the >75%-Group reported fewer days of psychosocial problems and cocaine use than counterparts (p's<.001 to .004).
Conclusions: Future pharmacotherapy clinical trials might consider 75% negative urine specimens as a threshold for defining treatment responders.
Financial Support: R33DA041661 (PI: Kiluk)

ORAL COMMUNICATION: RACIAL DISPARITIES AND SUDS

STRUCTURAL RACISM IN THE OPIOID EPIDEMIC: DIFFERENTIAL OUTCOMES FOR OPIOID RELATED SYSTEMS BY RACE AMONG YOUNG ADULT USERS IN NEW YORK CITY

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Research on the opioid epidemic has focused on white opioid users often to the exclusion of Black opioid users. In this study, we use theories of structural racism to empirically test whether differential outcomes exist across opioid related institutional domains.
Methods: As part of a larger study consisting of structured interviews with 539 young adult opioid users ages 18–29 recruited via respondent-driven sampling (RDS), this analysis is based on a subsample of 120 opioid non-injectors. We explore outcomes within four subsystems related to the opioid epidemic: access to opioid prescriptions, drug treatment and harm reduction services, and contact with the criminal justice system. We employed four separate statistical models within each institutional system using bivariate, negative binomial regression, and logistic regression to explore if White and Black non-injectors present similar outcomes within each system. Adjusted models included social demographics (race, gender, household income) and other theoretically informed variables as covariates (healthcare access; taking opioids for pain relief; willingness to engage in drug treatment; and past overdose incidents).
Results: We found significant racial disparities for non-injectors across systems, with non-Hispanic Blacks (N=36) being less likely than non-Hispanic Whites (N=84) to receive medical opioid prescriptions (IRR -2.370, p=.001); less likely to attend short- and long-term drug treatment programs (AOR -3.693, p=.002); and spending more time incarcerated in their lifetime (IRR 3.650, p<0.001); adjusting for covariates. None of the Black participants (0%) had received methadone treatment, in contrast with Whites (22.6%).
Conclusions: Racial disparities for Blacks non-injectors, in comparison to Whites, exist across opioid related systems which could have pernicious effects on their ability to overcome opioid dependency. Other studies ought to explore how structural racism might prevent the appropriate prevention efforts for Black opioid users.

FACTORS RELATED TO TREATMENT RETENTION AND SUCCESS AND OUTCOME REPORTING FOR AFRICAN AMERICAN METHADONE PATIENTS: A SYSTEMATIC REVIEW

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human
Abstract Category Literature Review
Aim: Opioid use disorder (OUD) affects roughly 2 million people in the US. African Americans continue to be disproportionately represented in the criminal justice system, and experience broad disparities in healthcare quality and outcomes. Methadone is the most used medication for OUD among African Americans. This systematic review seeks to summarize the literature on RCTs initiating methadone in samples with significant representation of African American methadone patients; specifically analyzing factors related to treatment retention and outcomes.
Methods (Optional): Systematic review of electronic databases. Eligible studies were: (a) published in English; (b) before 08/2021; (c) conducted in the US; (d) RCTs focused on initiation of methadone in carceral or community settings; with samples comprised of (e) adult participants (all >18 years) and (f) at least 50% African American.
Results (Optional): There were 31 publications that fit inclusion criteria. Most of the reports originated in Baltimore MD (28), with the rest coming from Philadelphia and Chicago. Publications ranged in time from 1977-2021. Higher dose and older age were factors related to treatment retention. The most common outcomes reported in these publications were illicit opioid use, days in treatment, time to enter treatment, death, arrests, illicit drug use, and illegal activity. Studies were able to conclude that methadone was an effective treatment for OUD regardless of setting. Carceral initiations helped to reduce recidivism in initial follow-ups, but did not reduce recidivism through longer-term follow-ups. None of the RCTs explicitly compared outcomes by race/ethnicity.
Conclusions: Higher methadone dose and older age were associated with better outcomes including treatment retention. Men tended to remain in treatment longer, however, women were underrepresented (or entirely absent) in several studies. Most studies took place in Baltimore, which may limit generalizability to other locales. Few studies reported patient-centered outcomes (e.g., quality of life) which needs to be further studied in relation to treatment success.

RACIAL DIFFERENCES IN THE ASSOCIATION BETWEEN SOMATIC SYMPTOMS AND OPIOID MISUSE AMONG JUSTICE-INVOLVED ADOLESCENTS

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Drug Category Opiates/Opioids
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid misuse among health disparity populations is among the leading public health concerns in the United States. Justice-involved adolescents (JIA) are more prone to trauma, physiological pain, and substance misuse than adolescents in the general population. Somatic complaints may be linked to nonmedical and illicit opioids use among JIA. Evidence suggests that the impact of somatic complaints on risk for opioid misuse may be greater among JIA who are Black and Latinx due to having less access to prescription medicine and diversion networks than White adolescents. No prior study investigated racial differences in the relationship between somatic symptoms and opioid misuse among JIA.
Methods: Stratified logistic regression was employed to analyze a statewide sample of 79,960 JIA from the Florida Department of Juvenile Justice. This sample represents all youth who received one or more arrests for delinquency, completed the full intake assessment, and reached the age of 18 by the year 2016. Past 30-day opioid misuse and somatic complaints were both derived from self-reported data collected during standardized intake interviews.

Results: Compared to White JIA, Black adolescents had 92% lower odds of opioid misuse, and Latinx adolescents had 70% lower odds. For a one-unit increase in the somatic episodes, JIA had 72% higher odds of opioid misuse in the total sample. In regard to racial differences, experiencing three or four somatic episodes was associated with 2.6 times higher odds of opioid misuse among White JIA, 4.7 times higher odds among Black JIA, and 2.8 times higher odds among Latinx JIA compared to JIA that had no somatic episodes, respectively.
Conclusions: Programs that invest in access to affordable and responsible pain management may reduce opioid misuse. Health equity may curb opioid deaths among Black individuals by ensuring that somatic complaints are interpreted and treated appropriately across racial groups.
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IDENTIFYING DIFFERENCES BY RACE AND ETHNICITY: THE EFFECT OF ACA ON MEDICATION FOR OPIOID USE DISORDER (MOUD) USE AMONG HISPANIC/LATINX CLIENTS WHO USE OPIOIDS

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: The opioid overdose death rate increased 170% between 2014 and 2017 among Hispanic/Latinx people in the United States. Medication for opioid use disorder (MOUD) decreases the risk of fatal overdose among people who use opioids, but studies have shown racial and ethnic disparities in access. Understanding the impact of policies such as the Affordable Care Act (ACA) may be critical for responding to rising overdoses. Using Treatment Episode Data – Admissions (2007-2019), we estimated the effect of ACA implementation on MOUD use among Hispanic/Latinx clients by race.
Methods: We performed logistic and difference-in-difference analysis with state fixed effects to estimate changes of MOUD use after ACA implementation among 99,085 first treatment ambulatory visits by adult Hispanic/Latinx clients whose primary reason for treatment was opioid use. To put those findings in context, we also analyzed 548,771 Non-Hispanic Black or White clients. ACA implementation was the treatment variable, Hispanic/Latinx race (Asian, Black, Multiracial, Native American, White [reference group] or Only Hispanic/Latinx) was the group variable, and their interaction was the variable of interest.
Results: Unadjusted MOUD rates for all Latinx/Hispanic clients rose from 50.2% pre-ACA to 63.5% post-ACA. After ACA implementation, Hispanic/Latinx clients were 1.4 times more likely to access MOUD (AOR:1.44, 99th CI=[1.31, 1.56]), a smaller odds increase than non-Hispanic White clients (AOR=1.67, CI=[1.61, 1.74]) and non-Hispanic Black Clients (AOR=2.10, CI=[1.88, 2.29]). Using White Hispanic/Latinx as a reference group, we found significant changes in MOUD for Hispanic/Latinx clients by race: Native American (DID=0.09, CI=[0.02,0.16]), Only Hispanic/Latinx (DID=0.10, CI=[0.08,0.12]), Multiracial (DID=0.13, CI=[0.09,0.17]) and Asian (DID:-0.07, CI=[-0.13,-.01]) clients.
Conclusions: ACA implementation was associated with increased MOUD among the Hispanic/Latinx population, an effect that differed by race. Understanding differences in MOUD access by race among Hispanic/Latinx people will help identify specific interventions that may improve uptake of treatment for Hispanic/Latinx subgroups who use opioids.
Financial Support: Herrera, 1R36MH126473-01A1
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Choi, R61/33DA049252

ORAL COMMUNICATION: THE ROLE OF ANXIETY IN SUDS

SCREEN-MEDIA-RELATED BRAIN STRUCTURAL COVARIATION IS ASSOCIATED WITH LEVELS OF INTERNALIZING TWO YEARS LATER IN THE ABCD COHORT: IMPLICATIONS FOR SUBSTANCE-USE RISK

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Drug Category Other, Substance-use risk
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: Engaging in screen media activity (SMA) is common among children and adolescents. Some SMA (e.g., problematic internet use) has been linked to substance-use problems in adolescents and adults. Although cross-sectional studies have associated high SMA with structural brain patterns, it remains unclear whether levels of SMA may impact brain structural development and potential risk factors for substance use longitudinally. We aimed to investigate SMA/brain-structure relationships using longitudinal data from the Adolescent Brain Cognitive Development (ABCD) study.
Methods: ABCD participants with usable baseline (T1) and two-year follow-up (T2) structural imaging (N=5329; 2458 girls) were analyzed. We first used Joint and Individual Variation Explained (JIVE) to identify brain structural co-developing pattern(s) among 221 brain features (i.e., differences in surface area, thickness, or cortical and subcortical gray-matter volume between T1 and T2). Then, the identified co-developing patterns were used in generalized linear mixed-effect models to investigate associations with SMA and internalizing and externalizing psychopathology.
Results: An SMA-associated thalamus-prefrontal-cortex-brainstem structural co-variation pattern was identified which included gray-matter volume in brainstem, bilateral thalamus proper, gray-matter volume and/or cortical thickness in bilateral superior frontal gyrus, rostral middle frontal, inferior parietal, and inferior temporal regions. Subsequent regression analyses showed that this component was associated with baseline SMA (p-value=0.038, Effect size η^2=0.001) and internalizing psychopathology (p-value=0.016, Effect size η^2=0.001) at T2, respectively.
Conclusions: Baseline SMA was associated with subsequent brain structural co-development and internalizing behaviors at T2, with small effect sizes. These findings are consistent with longitudinal associations between distinct structural brain patterns and SMA and that these structural associations can be relevant for internalizing psychopathology in youth, a risk factor for subsequent substance-use problems.
Financial Support: Children and Screens, NIMH, NIAAA

ASSOCIATIONS BETWEEN ADOLESCENT INTERNALIZING BEHAVIOR AND ALCOHOL USE: THE MODERATING ROLE OF RASH IMPULSIVITY AND SEX, AND THE LINK WITH FUTURE ALCOHOL USE DISORDER

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Drug Category Alcohol
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Aim: Internalizing behavior is theorized to be associated with adolescent drinking (and in turn, alcohol use disorder (AUD)), via a tendency to drink to self-medicate. Empirically, however, the link between internalizing behavior and adolescent drinking is mixed, pointing to the existence of moderating factors. Namely, internalizing behavior may be associated with drinking, only among adolescents who tend to act without thought of consequences (i.e., have elevated levels of rash impulsivity), as this serves to negate fears of negative consequences seen among adolescents with elevated internalizing behavior. Further, given rash impulsivity is a more pronounced risk factor for drinking among adolescent girls, sex may further moderate the association between internalizing behavior and drinking.

Methods: Methods: This study used prospective data from the Quebec Longitudinal Study of Child Development (N=1,545, 52% female). Internalizing and rash impulsivity were assessed at 13 years, while AUD was assessed at 20 years. Growth curve modelling was used to examine drinking across adolescence, assessed at 13, 15, and 17 years.
Results: Results: The two-way interactions between internalizing behavior and rash impulsivity, and internalizing behavior and sex, were significantly associated with drinking frequency at 13 years. Namely, internalizing behavior was only associated with drinking frequency, when participants had high (□=0.122, 95%CI[0.038, 0.206]) but not low (□=-0.047, 95%CI[-0.123, 0.030]) rash impulsivity. Further, controlling for impulsivity, internalizing behavior was only associated with drinking frequency (13 years) among girls (□=0.105, 95%CI[0.033, 0.176]), but not boys (□=-0.035, 95%CI[-0.120, 0.049). Finally, internalizing behavior (13 years) was indirectly associated with AUD (20 years), via alcohol use frequency at 13 years (among adolescents high in rash impulsivity: indirect effect=0.030, 95%CI[0.006, 0.056]; among girls: indirect effect=0.028, 95%CI[0.006, 0.052]).
Conclusions: Conclusions: Findings highlight the need for targeted early interventions (<13 years) for girls with elevated internalizing and boys with elevated rash impulsivity and internalizing, to decrease likelihood of future AUD.
Financial Support: Nina Pocuca is supported by a Canadian Institute of Health Research Fellowship (MFE-176629)

A PILOT STUDY OF PROLONGED EXPOSURE THERAPY FOR INDIVIDUALS WITH CONCURRENT POSTTRAUMATIC STRESS DISORDER AND OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Posttraumatic stress disorder (PTSD) frequently co-occurs with opioid use disorder (OUD). Prolonged exposure therapy (PE) is a first-line treatment for improving PTSD symptoms. However, the efficacy of PE is often limited by poor attendance among individuals with substance use disorders. We are piloting subjects in a 12-week pilot study examining the initial feasibility of a protocol for improving PE attendance and PTSD symptoms among patients receiving medications for OUD (MOUD) with a concurrent diagnosis of PTSD.
Methods: Thus far, 17 buprenorphine- or methadone-maintained adults with PTSD have been randomized to receive either: a.) MOUD as usual (n=6), b.) MOUD+PE (n=5), or c.) MOUD+PE with attendance-based incentives (MOUD+Enhanced PE; n=6). PE consists of 12 weekly 60-minute sessions. The MOUD+Enhanced PE group also receives monetary incentives delivered contingent upon completion of PE sessions (max $920). In response to the ongoing COVID pandemic, we permitted PE sessions to be conducted via telemedicine or in-person. Primary outcomes include percentage of sessions attended and PTSD symptom severity.
Results: Promising preliminary data indicate that participants randomized to receive MOUD+Enhanced PE are more likely to attend PE sessions compared to those randomized to MOUD+PE (90% vs. 13% of sessions attended). The MOUD+Enhanced PE group has attended more telemedicine-delivered (100% vs. 15%) and in-person (88% vs. 8%) PE sessions vs. the MOUD+PE group. Furthermore, the MOUD+Enhanced PE group has shown promising improvements in PTSD symptoms between intake and week 12. Formal statistical comparisons with a larger sample size will be presented at the June meeting.
Conclusions: Preliminary findings from this pilot study are very promising and indicate that participants who are receiving attendance-based monetary incentives have attended more PE sessions than non-incentivized participants. Furthermore, participants randomized to MOUD+Enhanced PE are demonstrating promising reductions in PTSD symptoms. Additional work is needed to examine the efficacy of MOUD+Enhanced PE relative to MOUD alone.
Financial Support: National Institute of General Medical Sciences (P20GM103644)

EXPOSURE OF ADOLESCENTS TO SECONDHAND SMOKE AND ITS ASSOCIATION WITH ANXIETY, DEPRESSION AND SUSCEPTIBILITY TO SMOKING IN LAGOS, NIGERIA

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Drug Category Nicotine/Tobacco
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: This study aimed to assess the prevalence of self-reported anxiety, depression and susceptibility to smoking as well as their relationship with exposure to SHS among adolescents in Lagos, Nigeria.
Methods: A cross-sectional study among non-smoking adolescents using an interviewer administered questionnaire was conducted. The survey had five sections: sociodemographic information, history of exposure to SHS, the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder - 7 (GAD-7) which were used to assess self-reported depression and anxiety and Susceptibility to smoking cigarettes which was assessed using a composite index of three questions. Multivariable logistic regression was used to examine the relationship between predictor and outcome variables. Statistical analysis was done using SPSS 26.0 software. P-values <0.05 were considered significant
Results: Of the 300 adolescents surveyed (mean age 12.9±1.43), 7.6 % were regularly exposed to SHS, of which 3.0% were daily exposed to SHS indoors. The prevalence of self-reported anxiety and depression were 29.6% and 11.0% respectively while the prevalence of susceptibility to smoking was 16.2%. In the bivariate analysis, females (p=0.022), those living in crowded accommodations (p=0.020), and those <5years of age when their caregivers started smoking indoors (p=0.001) had significantly higher exposure to SHS. In multivariable analyses, indoor SHS exposure for ≥ 1 hour daily was associated with increased odds for susceptibility to smoking (aOR = 3.793; 95%-CI: 0.98–14.60; p= 0.052) and increased odds for anxiety (aOR = 1.303; 95%-CI: 0.84–2.01; p= 0.228) and slightly reduced odds for depression (aOR = 0.952; 95%-CI: 0.62–1.47; p= 0.822).
Conclusions: SHS exposure was associated with higher odds of susceptibility to smoking and of anxiety possibly moderated by factors such as age at onset of exposure to SHS, female gender and type of accommodation. Longitudinal studies are however required to determine the nature and direction of the association.

ORAL COMMUNICATION: IMAGING RESEARCH WITH NICOTINE

NICOTINE DEPENDENCE AND FUNCTIONAL CONNECTIVITY OF INSULAR CORTEX SUBREGIONS

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: The insular cortex has been identified as a promising target in brain-based therapies for Tobacco Use Disorder, and has three major sub-regions (ventral anterior, dorsal anterior, and posterior) that serve distinct functional networks. Distinctions have been made between insular subregions with respect to resting state functional connectivity (RSFC) in the brain and symptoms of nicotine withdrawal. How subregions of the insula and associated networks contribute to nicotine dependence has not been well understood, and therefore was the subject of this study. Given the patient and neuroimaging literature, we hypothesized that anterior subregions would be more associated with nicotine dependence than posterior regions.
Methods: Sixty individuals (28 female, 32 male; age: 18-45 years old, mean=32.8) who smoked cigarettes daily (11.7±5 cigarettes/day) gave self-reports on the Fagerström Test for Nicotine Dependence (FTND) (score: 4.1 ± 2.1). After abstaining from smoking overnight (~12 h), as verified by CO in expired air

<10ppm, they underwent functional MRI to measure RSFC. Correlations between FTDN score and RSFC of the major insular sub-regions were evaluated using whole-brain-corrected voxel-wise analyses (voxel height: Z>3.1, cluster correction: P<0.05) and post-hoc region-of-interest (ROI) analyses.
Results: Nicotine dependence was negatively correlated with connectivity of both the right dorsal and left ventral anterior insula with the left precuneus. In post-hoc ROI analyses, nicotine dependence correlated negatively with connectivity between all anterior insula subregions and the left precuneus (P<0.05).
Conclusions: These results suggest the importance of the anterior insula-precuneus functional network for nicotine dependence, with greater nicotine dependence linked to weaker connectivity. The precuneus has been associated with dependence of both nicotine and alcohol. Therefore, this network may be a strong candidate for therapeutic approaches, such as brain stimulation, to target.
Financial Support: National Institute on Drug Abuse (NIDA) (R37 DA044467), Thomas P. and Katherine K. Pike Chair in Addiction Studies and the Marjorie M. Greene Trust.

RECONFIGURATION OF STRIATAL CONNECTIVITY PROFILES IN SMOKERS

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Corticostriatal circuits are central to reward processing and reinforcement learning functions that become dysregulated in substance use disorder (SUD) and drive compulsive drug use. Striatal nodes receive appreciable input from many cortical nodes, and their activity is shaped more by the combinational features of their multivariate connectivity profiles than by connectivity with any individual cortical node. Thus, the ability to detect and characterize significant reconfigurations in striatal connectivity profiles related to SUD may provide deeper insights about the sites most central to the etiology and maintenance of SUDs.
Methods: We introduce a Connectivity Profile Analysis (CPA) approach for quantifying and statistically evaluating different types of functional connectivity profile reconfigurations (i.e., aggregate divergence, rank order rearrangement, and entropy shift) and apply it to nicotine dependent smokers (n=46, 58.7% male) during smoking satiety and acute abstinence and matched non-smokers (n=33).
Results: First, smoking-related connectivity profile reconfigurations differ in both type and state-dependency in dorsolateral versus ventromedial striatum. However, the right caudal ventral putamen uniquely displays both "trait" rank order rearrangement and "state-dependent" aggregate divergence. Here, connections with cognitive cortical areas overtake those with motor/premotor cortical areas as the strongest in the connectivity profile (p<0.001), and abstinence significantly magnifies this rearrangement (p<0.001). Further, the interactive magnitude of these two reconfiguration types is significantly negatively associated with nicotine dependence severity (p<0.05). Circuit reconfigurations at this site may therefore reflect compensatory changes that attenuate drug-seeking in the absence of nicotine.
Conclusions: In sum, we identify a unique striatal site - implicated previously in the control of habitual behaviors - where the extent to which trait circuit reconfigurations are magnified by state circuit reconfigurations during acute abstinence is linked to dependence severity. Findings underscore the need for increased examination of connectivity profile reconfigurations as a mechanism of SUD etiology and as a potential guide for identifying therapeutic intervention targets.
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ANTERIOR CINGULATE GLUTAMATE, NICOTINE DEPENDENCE AND SEX DIFFERENCE: A BRAIN IMAGING STUDY

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Drug Category Nicotine/Tobacco
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: Aim: Glutamate concentration in some brain regions differs by sex and may affect smoking-related behaviors; thus, interventions that change regional glutamate levels may differentially influence smoking-cessation in men and women. We tested whether glutamate in the dorsal anterior cingulate cortex (dACC), a brain region implicated in smoking-related states, differs by sex and is related to nicotine dependence and tobacco withdrawal.
Methods: Methods: Men (N=30) and women (N=31), 18-45 years old, who reported smoking at least 4 cigarettes/day, provided self-reports on the Fagerström Test for Nicotine Dependence. After overnight abstinence from smoking, verified by CO <10 ppm, withdrawal was measured using subscales of the Schiffman-Jarvik Withdrawal Scale (SJWS) and glutamate was measured by proton magnetic resonance spectroscopy (1H-MRS) after a structural scan (MPRAGE) for dACC voxel positioning. MRS spectra were fit using SVFit software. In women, serum levels of 17β-estradiol and progesterone were determined using electrochemiluminescence immunoassays.
Results: Results: Glutamate in the dACC correlated negatively with nicotine dependence (p=0.046). In women, glutamate was lower than in men (p=0.04) and was negatively correlated significantly with 17β-estradiol (p=0.039) and non-significantly with progesterone (p=0.052). There also was a negative correlation of dACC glutamate with sedation, but not other subscales of the SJWS, in women only (p=0.011).
Conclusions: Conclusions: Interventions to elevate dACC glutamate may be helpful for smoking cessation and may ameliorate sedation linked to tobacco withdrawal, especially in women. Periods of hormonal transitions (e.g., menstrual cycle, menarche, menopause) may present unique vulnerabilities for relapse or opportunities for cessation if it is confirmed that ovarian hormones interact with glutamate to influence smoking behavior. Ongoing studies are evaluating the effects of acute smoking and are incorporating assessments of participants who do not smoke to evaluate the extent to which the observed differences in dACC glutamate and associations with ovarian hormone levels are restricted to individuals who smoke.
Financial Support: This research was supported, in part, by a grant from the National Institute on Drug Abuse (NIDA) (R37 DA044467, EDL) and endowments from the Thomas P. and Katherine K. Pike Chair in Addiction Studies and the Marjorie M. Greene Trust (EDL). Dr. Perez Diaz is supported by a Ruth L. Kirschstein Postdoctoral Individual National Research Award from NIDA (F32 DA049500-01A1). We acknowledge the Canada Research Chairs program (Dr. Tyndale, the Canada Research Chair in Pharmacogenomics). Dr. Tyndale has consulted for Quinn Emanuel and Ethismos Research Inc. All other authors declare no conflicts of interest.

STRESS- AND CUE-INDUCED BRAIN ACTIVATION AND RELAPSE IN CIGARETTE SMOKERS UNDERGOING SMOKING CESSATION TREATMENT: A PROSPECTIVE FMRI STUDY

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Tobacco use disorder is characterized by high relapse rates in recently abstinent smokers. Research has demonstrated reactivity to stress and to cue exposure to be major determinants for relapses. Few studies have examined the potential neural mechanisms associated with stress- and cue-induced relapse. This study was a pilot fMRI investigation of regional brain activation in response to laboratory stress and cigarette-smoking cues as they relate to relapse in cigarette smokers undergoing treatment.
Methods: 18 participants with tobacco use disorder (>15 cigarettes daily for >2 years) underwent a 6-month cognitive behavioral therapy for smoking cessation. Prior to treatment, all participants completed fMRI stress and cue exposure tasks. Whole-brain fMRI contrasts were performed separately between stress induction (mental arithmetic) versus non-stress (counting), and smoking-cue versus neutral non-drug (video clips). Self-reported craving was assessed after cue exposure. Data were compared between participants who relapsed versus abstained during treatment.

Results: 9 participants abstained from cigarette smoking (40.3 ± 7.4 years old; 4F) compared to 9 who relapsed (38.9 ± 6.9 years old; 6F). During cue exposure those who relapsed showed increased activation in the superior parietal cortex, fusiform gyrus, anterior cingulate, dorsolateral prefrontal cortex, orbitofrontal cortex, and pre-supplementary motor area relative to abstainers, with no differences between self-reported craving in response to cues. Under stress, individuals who relapsed exhibited greater activation in the fusiform gyrus, dorsolateral prefrontal cortex, orbitofrontal cortex, cerebellum, and anterior insula.
Conclusions: Findings show overlapping and differential brain region involvement during stress- and cue-related responding contributes to cigarette use relapse. These data suggest clinically relevant neural substrates are distinguishable for the well-established relapse risk factors of exposure to stress and drug cues. Future broader investigations are needed to confirm findings as well as to investigate stress- and cue-related neural activation and relapse among users of other drugs.
Financial Support: Funding support for this study was provided by the National Institutes of Health

ORAL COMMUNICATION: METHAMPHETAMINE CLINICAL RESEARCH

OUTCOMES AND MEASURES USED IN RANDOMISED CONTROLLED TRIALS EXAMINING PHARMACOTHERAPIES FOR THE TREATMENT OF METHAMPHETAMINE WITHDRAWAL: RESULTS OF A SYSTEMATIC REVIEW

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Cessation of methamphetamine (MA) use may result in a characteristic withdrawal syndrome and no medication has been approved for this indication. Harmonised outcomes and methods to measure them enhances the capacity to meta-analyse data and increase generalisability.
Methods: MEDLINE (1966-2020), CINAHL (1982-2020), PsychINFO (1806-2020) and EMBASE (1947-2020) were systematically searched. Studies were included if they were randomised controlled trials (RCTs) investigating pharmacological treatments for MA withdrawal. The selected studies were evaluated for outcome measures, which were any reported impact related to the treatment of MA withdrawal.
Results: Nine RCTs of 6 medications, collectively enrolling 242 participants met inclusion criteria. Mean sample size across studies was 27 participants, and 88% of participants were male. Six studies (67%) reported retention to primary outcome, with 51 (27%) participants not retained to treatment completion. In total 12 primary outcome measures were reported (some studies assessed their primary outcome with multiple measures), used 14 times across studies. The most common outcome measures were the Amphetamine Withdrawal Questionnaire, Continuous Performance Test-II and retention to study intervention (2 studies [22%] each). Seventeen secondary outcome measures were assessed across studies, most commonly investigating withdrawal symptoms including craving, mental health, and sleep outcomes.
Conclusions: Definitions of efficacy of pharmacotherapies vary extensively. While some studies define success by reduction in withdrawal symptoms, others consider changes in attention ability or retention in treatment to define treatment success. This is particularly concerning due to the lack of validated measures available for the measurement of MA withdrawal outcomes, and a lack of consensus in the literature regarding what a “successful” withdrawal looks like. Clinical researchers can benefit from selection of outcomes and measures that comport well with the literature to enhance the contextual placement of their research, improve sector-wide ability to systematically review data and generalise results across studies that often have under-powered samples.

NALOXONE IS LESS EFFECTIVE AT REVERSING CARDIOVASCULAR EFFECTS OF FENTANYL-METHAMPHETAMINE MIXTURES THAN FENTANYL ALONE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)

Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Over the past decade, opioid-related deaths have increased exponentially, however, overdose deaths attributed to stimulants (e.g., methamphetamine) have also increased sharply. Moreover, there is a growing realization that many of these deaths involved both opioids and stimulants. Despite these alarming trends, little is known about the toxidrome of mixtures of opioids and stimulants. The current studies aimed to characterize the cardiovascular effects of opioids, stimulants, and opioid + stimulant mixtures, and to determine the effectiveness of naloxone to reverse these effects.
Methods: Male Sprague Dawley rats (n=8) were implanted with a radiotelemetric probe, and a femoral catheter to allow for intravenous drug delivery. Dose-response curves for the effects of fentanyl (0.001-0.56 mg/kg), and methamphetamine (0.1-3.2 mg/kg) on heart rate and blood pressure were generated before evaluating the effects of a mixture of fentanyl (0.56 mg/kg) and methamphetamine (1 mg/kg). Finally, naloxone (1 mg/kg and 3.2 mg/kg) was administered as a 5-min post-treatment to determine its effectiveness to reverse the cardiovascular effects of fentanyl, methamphetamine, and mixtures of fentanyl + methamphetamine.
Results: Fentanyl produced a dose-related bradycardia and hypotension, whereas methamphetamine produced a dose-related tachycardia and hypertension. When co-administered, fentanyl and methamphetamine produced a significant bradycardia and hypotension. Naloxone rapidly reversed the cardiovascular effects of fentanyl but was less effective at reversing the cardiovascular effects of a mixture of fentanyl + methamphetamine. Naloxone did not impact tachycardia or hypertension produced by methamphetamine.
Conclusions: These studies suggest that concurrent use of opioids (fentanyl) and stimulants (methamphetamine) can result in an enhanced cardiovascular response. Additionally, although naloxone produced a rapid and full reversal of the cardiovascular effects of fentanyl, the fact that it was unable to reverse the effects of a mixture of fentanyl + methamphetamine suggests that alternate strategies are needed to address the growing number of overdoses related to co-use of opioids and methamphetamine.
Financial Support: This work was supported by NIH/NIDA grant R01 DA039146.

STAMPOUT: IMPACT IN HUMANS OF IXT-M200 (A HIGH-AFFINITY METHAMPHETAMINE ANTIBODY) ON METHAMPHETAMINE CONCENTRATIONS AND EFFECTS

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of STAMPOUT was to determine the safety, tolerability, and pharmacokinetics (PK) of single IV doses of IXT-m200, a high-affinity, anti-methamphetamine (METH) antibody, followed by weekly IV METH challenges in subjects with METH use disorders. IXT-m200 impacts on METH PK and effects as measured by drug effects questionnaires (DEQ) were determined.
Methods: This was a parallel-group, placebo-controlled, double-blind study in non-treatment-seeking participants. Subjects discriminated METH (30 mg, IV) from placebo with DEQ to qualify. Qualifiers received a single dose of IXT-m200 (6 or 20 mg/kg) or placebo followed by weekly METH challenges for up to 4 weeks. The challenges consisted of METH and placebo, separated by 4 hr. Safety, METH and IXT-m200 PK, and DEQ data were collected for up to 126 days.
Results: Twenty subjects received IXT-m200 placebo; 18 received 6 mg/kg and 18 received 20 mg/kg IXT-m200. IXT-m200 was well-tolerated. There were no SAEs and all AEs were grades 1 and 2; all resolved. Most AEs were expected sequelae of METH.
IXT-m200 significantly ($p<0.001$) altered METH AUC and Cmax with all METH challenges, up to 30-fold and 8-fold respectively, without altering METH renal elimination. IXT-m200 decreased METH Vd over 9-fold after the first METH challenge. METH Vd remained significantly reduced after each METH challenge by up to 40 (6 mg/kg) and 78% (20 mg/kg) at 3 weeks after IXT-m200 dosing.

The DEQ data were highly variable, precluding statistical significance on many endpoints. Several DEQ parameters, however, approached or achieved statistical significance. These data suggest that METH redistribution by IXT-m200 may reduce METH CNS effects.
Conclusions: IXT-m200 successfully achieved the primary endpoint in STAMPOUT, alteration in METH PK ($p<0.001$). IXT-m200 was well-tolerated in METH users given METH challenges following a single IXT-m200 dose, and demonstrated an acceptable safety profile supportive of further development.
Financial Support: NIDA: U01DA045366

UTILITY OF A CONTROLLED AMPHETAMINE WITHDRAWAL PARADIGM AMONG ADULTS WHO USE METHAMPHETAMINE: A PILOT CLINICAL TRIAL

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: The continued increase in prevalence of methamphetamine use in the United States has resulted in a significant increase in the number of patients entering treatment for methamphetamine use. However, no robustly efficacious pharmacologic treatment for methamphetamine use or withdrawal after stopping methamphetamine use has been identified to date. Given the association between methamphetamine withdrawal and relapse during early treatment, this study tested a controlled d-amphetamine withdrawal paradigm among methamphetamine-using individuals.
Methods: Treatment-seeking adults who used methamphetamine (N=34; 47% female; 100% white) were enrolled in a four-week, randomized, double-blind, placebo-controlled trial in a residential setting, in which all participants were maintained on d-amphetamine (30 mg BID) during week 1, then half were switched to placebo during weeks 2-3. All participants received placebo during week 4. Outcomes included vital signs, withdrawal, cravings for methamphetamine, mood, and cognition. Bivariate analyses tested treatment group differences on baseline demographic and outcome variables. Repeated measures models examined main and interaction effects of treatment over time.
Results: Participants were successfully randomized and safely stabilized on d-amphetamine. Craving for methamphetamine increased during weeks 2-3 in the placebo group relative to those on d-amphetamine. Interactions with age and heart rate were noted.
Conclusions: To our knowledge, this is the first double blind, placebo-controlled trial measuring pharmacologic effects of abruptly stopping controlled d-amphetamine administration in adults who use methamphetamine. Results support the potential of this withdrawal paradigm to further examine the efficacy of pharmacologic agents in ameliorating methamphetamine withdrawal symptoms.
Financial Support: Research supported by NCRR-RR020146.

ORAL COMMUNICATION: ALCOHOL AND COPING BEHAVIORS

ADVERSE CHILDHOOD EXPERIENCES ARE ASSOCIATED WITH RISK PATTERNS OF ALCOHOL/CANNABIS CO-USE: A LONGITUDINAL STUDY IN PUERTO RICAN YOUTH

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Adverse childhood experiences (ACEs) are associated with alcohol and cannabis use in youth. Little is known about ACEs and alcohol/cannabis co-use especially among Puerto Rican youth, who often experience multiple ACEs. We examined the prospective relationship between ACEs and alcohol/cannabis co-use in Puerto Rican youth.

Methods: We included 2,004 participants from a longitudinal study of Puerto Rican youth originally recruited in the South Bronx (New York) and Puerto Rico. We assessed the relationship between eleven ACEs (e.g., parental loss, child maltreatment, parental maladjustment, and exposure to violence, categorized as 0-1, 2-3, and 4+ ACEs.) at waves 1-3 (2000-2004, ages 5-15, and alcohol/cannabis use patterns in the past month at wave 4 (2013-2017, ages 15-29). Our outcome variable was composed of 5 mutually exclusive categories of alcohol/cannabis use patterns: no lifetime use, low-risk (no binge-drinking episodes, cannabis use <10 times), binge-drinking only, cannabis use only (10+ times), alcohol/cannabis co-use (binge-drinking and cannabis use). We conducted weighted multinomial logistic regression to test associations between ACEs and alcohol/cannabis use, adjusting for sociodemographic variables.
Results: Reporting 4+ACEs in waves 1-3 (vs. 0-1 ACEs) was associated with greater odds of engaging in low-risk alcohol/cannabis use (aOR 1.80, 95% CI=1.12-2.88), binge-drinking only (aOR 1.74, 95% CI=1.04-2.91), cannabis use alone (aOR 3.65 95% CI=1.55-8.58) and alcohol/cannabis co-use (aOR 4.35, 95% CI=2.11-8.97) in wave 4 (reference category: no lifetime use). Furthermore, reporting 4+ ACEs (vs. 0-1 ACEs) was associated with 2.42 times higher odds (95% CI=1.28-4.58) of alcohol/cannabis co-use (vs. the low-risk alcohol/cannabis use category). No associations were seen between ACEs and cannabis use alone, ACEs and binge-drinking only, using low risk alcohol/cannabis use as a reference.
Conclusions: In Puerto Rican youth, prevention strategies to reduce risk patterns of alcohol/cannabis co-use should also focus on those experiencing 4+ACEs.
Financial Support: National Institute on Drug Abuse (NIDA) T32DA031099 (Hasin) and K08DA049913 (Sussman), National Institute of Health MH56401 (Bird), DA033172 (Duarte), AA020191 (Duarte), MH098374 (Alegria, Canino, Duarte), HD060072 (Martins, Duarte, Canino), HL125761 (Suglia), UG3OD023328-01 (Duarte, Canino, Monk, Posner).

COPING STYLE MODERATES RELATIONSHIP BETWEEN IMPULSIVITY AND PROBLEMATIC ALCOHOL USE IN DEPRESSED AND ANXIOUS INDIVIDUALS

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Research demonstrates a positive relationship between impulsivity and problematic drinking (Herman and Duka, 2019), and the strength of this association in addictive behaviors is influenced by coping style (Lightsey and Hulsey, 2002). The present study examined the moderating role of coping style on the relationship between impulsivity and problematic alcohol use.
Methods: Participants (N = 228) included adults with current depressive and anxiety symptoms (56% women; 58% white; mean age = 34.4 years, SD = 13.0; mean education = 15.8 years, SD = 2.2). Measures included the Barratt Impulsiveness Scale, AUDIT for problematic drinking, and the Brief-COPE inventory.
Results: Specific coping strategies ($p < .01$) significantly associated with problematic alcohol use included Denial ($r = .23$), Substance Use ($r = .72$); Religion ($r = .24$), Self-Blame ($r = .22$), and Informational Support ($r = .22$). In a linear regression analysis of moderation using SPSS v27, Emotion-Focused coping had a modest effect on the relationship between impulsivity and problematic alcohol use ($b = 0.018$, 95% CI, [0.001, 0.034], $t = 2.115$, $p = 0.036$), as did Avoidant coping ($b = 0.0$, 95% CI, [0.018, 0.063], $t = 3.573$, $p = 0.000$). Problem-Focused coping did not moderate the relationship.
Conclusions: These results suggest that individuals with depression and anxiety symptoms who endorse impulsivity traits show different levels of alcohol use based on their engagement in avoidant or emotion-focused coping. Findings also indicate that individuals who use alcohol or substances to cope with psychological distress may be at higher risk for developing alcohol problems. Assessment of coping styles in individuals with depression and anxiety symptoms may be warranted to identify problematic drinking. Interventions targeting the use of high avoidant and emotion-focused coping may be an important treatment consideration among individuals with depressive and anxiety symptoms.

PROSPECTIVE ASSOCIATIONS OF PSYCHEDELIC TREATMENT FOR CO-OCCURRING ALCOHOL MISUSE AND POST-TRAUMATIC STRESS SYMPTOMS AMONG UNITED STATES SPECIAL OPERATIONS FORCES VETERANS

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Drug Category Psychedelics
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Examine the prospective associations of ibogaine and 5-MeO-DMT treatment for risky alcohol use and post-traumatic stress disorder (PTSD) symptoms among United States (US) Special Operations Forces Veterans (SOFV).
Methods: Data were prospectively collected during standard clinical operations at pre-treatment and 1-month (1m), 3-months (3m), and 6-months (6m) post-treatment from September 2019 to March 2021 in an ibogaine and 5-MeO-DMT treatment program serving SOFV in Mexico. Data were analyzed to explore treatment effectiveness. Missing data were imputed (last known data point carried forward). PTSD symptoms were measured using the PTSD Symptom Checklist for DSM 5 (PCL-5). Of the 86 SOFV that completed treatment, 45 met criteria for risky alcohol use at pre-treatment (> 4 on the AUDIT-C; 4-5=Moderate risk [29%], 6-7=High risk [29%], 8-12=Severe risk [42%]) and were included in this analysis (Mean Age=44; male=100%; married=58%; Caucasian/White=91%; OEF/OIF Service=93%).
Results: There was a significant and very large reduction in alcohol use from pre-treatment (M=7.2, SD=2.3) to 1m (M=3.6; SD=3.5) post-treatment, which remained reduced through 6m after treatment (M=4.0; SD=2.9; p<.001, partial eta squared=.617). At 1m, 24% were abstinent, 33% were engaging in non-risky drinking, and 42% remained risky drinkers (18%=Moderate risk; 7%=High risk; 18%=Severe risk). At 6m, 16% were abstinent, 31% were engaging in non-risky drinking, and 53% remained risky drinkers (24%=Moderate risk; 16%=High risk; 13%=Severe risk). There were no differences between responders (abstinent/non-risky drinkers) and non-responders (risky drinkers) in pre-treatment demographics or clinical characteristics. However, at 1m decreases in alcohol use were significantly correlated with decreases in PTSD symptoms (r=.44; p=.003) and improvements in cognitive functioning (r=.44; p=.003), suggesting an attenuated response to treatment overall.
Conclusions: Given these findings, clinical trials should be conducted to determine whether psychedelic-assisted therapy holds promise for individuals with complex trauma and alcohol misuse who have not been successfully treated with traditional interventions.
Financial Support: Funding for this study was provided by Veterans Exploring Treatment Solutions. AKD and NS are supported by private philanthropic funding from Tim Ferriss, Matt Mullenweg, Craig Nerenberg, Blake Mycoskie, and the Steven and Alexandra Cohen Foundation. AKD, SBA, YX, and NS are supported by the Center for Psychedelic Drug Research and Education, funded by anonymous private donors. LAA is supported by the Department of Veterans Affairs (IK2-CX001873) and the American Foundation for Suicide Prevention. The funding sources had no role in the study, data analysis, interpretation, or communication of findings.

RELATIONSHIPS AMONG PTSD, TRAIT MINDFULNESS, AND FACTORS OF SUD IN VETERANS ENROLLED IN SPECIALTY SUD TREATMENT

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Mindfulness has been shown to have a role in the comorbidity between posttraumatic stress disorder (PTSD) and substance use disorders (SUDs). The primary goal of the current study was to investigate associations among PTSD, trait mindfulness, and factors of SUD in Veterans enrolled in SUD treatment.
Methods: Veterans enrolled in VA specialty SUD treatment program were recruited from group classes and waiting rooms. Participants completed survey measures assessing SUD-related factors of frequency of alcohol use, hazardous alcohol use, consequences from substance use, and craving, as well as PTSD symptoms, trait mindfulness, and depressive symptoms. Three hierarchical multiple regressions assessed

SUD-related factors associated with PTSD and mindfulness facets when controlling for other study variables.
Results: Study sample (n=159) was predominately male (91.2%) and white (86.2%) (age: M= 57.3; SD=12.9). Zero-order correlations showed significant relations among trait mindfulness facets, PTSD, and SUD-related factors. After controlling for demographic factors, PTSD, and clinical variables, trait mindfulness facets were associated with SUD-related factors; the observe facet was related to frequency of alcohol use ($p < .05$), non-judging was related to hazardous alcohol use ($p < .05$), and non-reactivity was associated with consequences from substance use ($p < .01$). Exploratory analyses suggest mindfulness factors mediated the relationship between PTSD and the SUD-related factors of hazardous alcohol use (indirect effect = -0.30, 95% CI [-0.73, -0.06]) and consequences from substance use (indirect effect = 0.99, 95% CI [0.39, 1.93]).
Conclusions: Trait mindfulness factors may help explain the relationship between SUD and PTSD. Nuanced relationships among mindfulness facets and SUD in those with PTSD may inform concurrent treatment of both disorders by enhancing the ability to attend to experience in a non-judgmental and non-reactive way through mindfulness training.

ORAL COMMUNICATION: MEANINGFUL INTERACTIONS WITH CANNABINOIDS

LOCOMOTOR AND ANALGESIC EFFECTS OF VAPED DELTA8-TETRAHYDROCANNABINOL, CANNABIDIOL AND MIXTURES IN MALE RATS

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Delta-8-Tetrahydrocannabinol (Delta-8) has the largest growth in sales in the 2021 cannabinoid market, although overall sales still trail cannabidiol (CBD). The current study was designed to develop a rat model of vaped Delta-8 and CBD to better understand the effects of these drugs individually and in combination.
Methods: Twelve male Sprague Dawley (PND 56) rats were exposed for 10 min to vapor generated from various doses of Delta-8 distillate (0, 10, 20 and 40 mg/.300 ml) or CBD isolate (0, 30, 60 and 120 mg/.300 ml) dissolved in propylene glycol, prior to being placed into locomotor boxes for 2 hrs. Following completion of the acute dose effect curves for Delta-8 and CBD, rats were then tested with different CBD:Delta-8 mixtures (60:20, 20:20 and 20:60 mg:mg/.300 ml). Finally, the analgesic effects of these compounds were tested with the warm-water tail withdrawal test.
Results: Delta-8 resulted in a relatively flat non-significant dose effect curve in distance traveled. CBD alone resulted in a significant dose dependent increase in locomotor behavior. Mixtures of the two drugs resulted in greater locomotor stimulation relative to Delta-8 alone but not CBD alone. A 20 mg/.300 ml of Detla-8 increased tail withdrawal latency 60-min post vape compared to vehicle. The 60 mg/.300 ml dose of CBD increased tail withdrawal latency at 0- and 60-min post vape although the CBD/Delta-8 mixture resulted in a significantly greater increase in latency compared to CBD alone at 0- and 30-min post vape.
Conclusions: The current study indicates that we can establish behaviorally active dosing using a vaped pulmonary route of administration and that Delta-8 alone does not significantly alter locomotor behavior, while vaped CBD and in combination with Delta-8 can increase locomotor behavior. We also found these drugs have a modest analgesic effect that is heighten when CBD and Delta-8 are combined.
Financial Support: Storz and Bickel supplied vaporizers and vaporizer supplies for this study.

INDIVIDUAL AND INTERACTIVE EFFECTS OF DELTA-9-TETRAHYDROCANNABINOL (THC) AND ALPHA-PINENE

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Drug Category Cannabis/Cannabinoids

Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: This controlled human laboratory study is evaluating whether the terpenoid alpha-pinene mitigates acute impairment of working memory ability commonly associated with administration of high doses of delta-9-tetrahydrocannabinol (THC).
Methods: Healthy adults (n=3) completed nine, double-blind, outpatient drug administration sessions. During each session, participants inhaled vaporized THC alone (15 or 30mg THC), vaporized alpha-pinene alone (0.5 or 5mg), or vaporized THC and alpha-pinene in combination (15mg THC/0.5mg pinene; 15mg THC/5mg pinene; 30mg THC/0.5mg pinene; 30mg THC/5mg pinene), or placebo. Outcomes assessed before and for 6 hours after drug administration included: working memory performance (Paced-Serial-Addition-Task, PASAT), encoding and retrieval of episodic memories via a delayed verbal recall test, psychomotor performance (Digit-Symbol-Substitution-Task, DSST), and subjective drug effects (Visual Analog Scales).
Results: As expected, THC qualitatively impaired working memory performance and was associated with subjective impairment of memory in all three participants. When THC was administered with the 0.5 and 5.0mg doses of alpha-pinene improved performance on the PASAT and the DSST was observed for one of three of the participants compared to when THC was administered alone with no effect in the other two. Further, in two of the three participants, retrieval of episodic memories during the delayed verbal recall test was improved when 30mg THC was combined with both doses of alpha-pinene compared with THC alone. Alpha-pinene reduced self-reported ratings of having “trouble with memory” and “difficulty with tasks” in one of three participants, with no effect in the other two. Alpha-pinene did not produce discriminable subjective drug effects or impact cognitive ability when administered by itself.
Conclusions: These preliminary data suggest that alpha-pinene may produce modest improvements in THC-induced memory impairments for some individuals, but additional data is needed to further elucidate the validity and reliability of this effect.
Financial Support: National Institute on Drug Abuse (NIDA) Grants R01-DA043475 and T32-DA007209

ANALGESIC AND ABUSE-RELATED EFFECTS OF VAPORIZED WITH VARYING CONCENTRATIONS OF DELTA-9-THC AND CBD IN HEALTHY VOLUNTEERS

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Cannabidiol (CBD) is hypothesized to both reduce adverse effects of delta-9-tetrahydrocannabinol (THC) and enhance its therapeutic effects. This double-blind, placebo-controlled study sought to probe the potential for inhaled CBD to increase THC-induced analgesic effects while reducing its abuse-related effects.
Methods: Healthy, cannabis-experienced participants were recruiting for this within-subject outpatient study (N = 10; 8 males, 2 females analyzed to date). Over 4 sessions, participants inhaled cannabis with THC (25 mg), CBD (25 mg), THC+CBD (25 mg each), or placebo (0 mg THC and CBD). Analgesic effects (i.e., pain tolerance) were determined using the Cold Pressor Test (CPT), and a cannabis self-administration task was used to assess abuse liability. For self-administration, participants were given the opportunity to purchase and self-administer up to 4 puffs of the cannabis they received in the morning at a cost of $2 per puff.
Results: CBD did not affect pain tolerance compared to placebo, whereas THC slightly increased pain tolerance (126.1 ± 8.7 vs. 105.7 ± 7.8 percent of pre-drug administration tolerance). The combination of THC and CBD had the most robust effect on pain tolerance (171.1± 41.0 percent of pre-drug administration tolerance, $p < 0.05$). For the self-administration task, 40% of participants chose to purchase ‘puffs’ of the cannabis they received earlier that session; more ‘puffs’ of THC+CBD were self-administered compared to placebo (2.0 ± 1.6 vs. 0.75 ± 0.95 puffs), THC alone (1.0 ± 1.4 puff), and CBD alone (0 puffs) ($p < 0.05$).

Conclusions: The current findings suggest that THC alone, as well as the combination of THC and CBD, increases pain tolerance (i.e., is analgesic); this latter condition was also the most self-administered, thus demonstrating the highest abuse liability of the three active cannabis conditions. Data collection and analyses are ongoing.
Financial Support: This study is supported by NIDA DA046614.

EXAMINATION OF MITRAGYNINE AND CANNABIDIOL INTERACTIONS: POTENTIAL SUBSTANCE USE DISORDER THERAPEUTIC

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Drug Interactions
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Drug overdoses continue to increase, so alternative therapies must be studied for their potential to aid individuals suffering from substance use disorders (SUD). Kratom, a southeast Asian plant, has been purported to mitigate opium withdrawal symptoms. Kratom's major chemical component is mitragynine (MTG). While cannabidiol (CBD), isolated from cannabis, decreases the rewarding effects of multiple drugs of abuse in preclinical models. This study aims to examine interactions between MTG and CBD as it relates to the development of novel SUD therapeutics.
Methods: Male and female Sprague Dawley rats (N=12) underwent both single- and multiple-dose administration of CBD + MTG. For single-dose study, rats were treated orally with 50 mg/kg CBD followed by 20 mg/kg MTG. For multiple-dose study, rats were treated twice daily with 25 mg/kg CBD + 10 mg/kg MTG for five days. A separate cohort of rats (N=8) were trained to discriminate MTG (32 mg/kg, oral) from vehicle under a standard two-lever operant conditioning procedure using food reinforcement. Once trained, rats were pretreated with CBD (50 mg/kg) 60 minutes prior to testing.
Results: After a single-oral dose with CBD pretreatment, the exposure of MTG increased 2-fold compared to MTG administered alone. At steady state, the exposure of MTG after CBD pretreatment was 4-fold greater than when MTG was administered alone. In drug discrimination studies, CBD produced a 12-fold leftward potency shift in male rats. Sex differences were observed in the pharmacokinetics and behaioral effects of CBD + MTG.
Conclusions: The results indicate CBD enhances MTG potency. Considering the potential of both compounds to treat SUD, a combination therapy of CBD and MTG will be further investigated. These results may help to develop a safe, effective, and accessible solution for those suffering from SUD.
Financial Support: This project is part of the University of Florida's "Creating the Healthiest Generation" Moonshot Initiative, which is supported by the UF Office of the Provost, UF Office of Research, UF Health, UF College of Medicine, and the UF Clinical and Translational Science Institute. Support was also obtained from the National Institutes of Health National Institute of Drug Abuse [Grants UG3 DA048353, UH3 DA048353, R01 DA047855], the University of Florida Foundation, and University of Florida Department of Pharmacodynamics Funding.

ORAL COMMUNICATION: BEHAVIORAL ECONOMICS

OVERHARVESTING IN SEQUENTIAL DECISION-MAKING RELATES TO DRUG ADDICTION AND A MARKER OF MIDBRAIN DOPAMINE FUNCTION IN HUMANS

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Drug Category Opiates/Opioids
Topic Behavioral Economics
Abstract Detail Human

Abstract Category Original Research
Aim: Addiction is marked by a tendency to exploit sources of reward despite diminishing returns. This behavior is captured by animal foraging models that have recently been extended to humans. Catecholaminergic systems have been theoretically linked to foraging behavior and are key neural substrates of addiction, yet a precise understanding of the relationship between foraging-type decision-making, addiction, and catecholamine function is lacking in humans. Thus we 1) measured how individuals with opioid use disorder (OUD) maximized reward based on the perceived richness of a given environment using an ecologically-valid patch-foraging framework, and 2) assessed whether individual differences in foraging behavior could be explained by the long-term function of catecholaminergic systems (dopamine, norepinephrine).
Methods: 42 OUD and 33 socio-demographically matched control participants completed a patch-foraging task, during which they made sequential decisions between "harvesting" a depleting "patch" for monetary rewards or incurring a cost to "travel" to a replenished patch. To assess catecholaminergic contributions to foraging behavior, in a subset of participants (n=53), we acquired high-resolution neuromelanin-sensitive MRI scans that were optimized to separately localize dopaminergic nuclei (substantia nigra, ventral tegmental area) and the noradrenergic locus coeruleus.
Results: All participants adaptively adjusted behavior to the long-running reward rate of the patch-foraging environments (P=0.0005; df=66.767). However, OUD participants stayed in reward patches longer than optimal (P=0.013995, df= 73.145)—markedly over-harvesting a reward source as its value declined—and this correlated with more chronic drug use (P=0.016836, df= 38.43). Imaging analysis revealed a dissociation whereby, across participants, over-harvesting was associated with lower neuromelanin signal contrast in the ventral tegmental area (P=0.0012214, df=52.941) but not in the locus coeruleus (P= 0.81413, df= 52.334).
Conclusions: Individual differences in foraging behavior are related to variability in dopaminergic—but not noradrenergic—function that informs reward rates in dynamic environments and may serve as a marker for maladaptive reward pursuit in addiction.
Financial Support: Rutgers Center for Alcohol and Substance Use Studies Pilot Award

BRAIN REACTIVITY BIAS TOWARD DRUG VERSUS PLEASANT CUES IS ASSOCIATED WITH DRUG DEMAND IN INDIVIDUALS WITH COCAINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The Late Positive Potential (LPP) is an electroencephalogram (EEG) component reflecting motivational relevance of a stimulus. Previous research indicates a brain reactivity bias, with larger LPPs to drug vs. pleasant (non-drug reward) images among some drug users. Drug demand is a behavioral economic measure assessing drug consumption as a function of increasing price and is used as a measure of motivation to use drugs. Despite these overlapping themes, no studies have compared this brain reactivity bias and drug demand among treatment-seeking individuals with cocaine use disorder (CUD).
Methods: Participants (N = 59) completed both a cocaine purchasing task and EEG picture viewing task at baseline. Comparisons between LPP and demand were conducted assessing: 1) basic associations between LPP difference wave amplitude (drug – pleasant) and demand indices (Q0, Omax, Pmax, essential value, breakpoint); and 2) exploratory cluster analyses classifying individuals into groups based on LPP cue response means (drug > pleasant; pleasant > drug; and other pattern). Bayesian GLM with weakly informative priors was used to quantify evidence (posterior probability ≥75%) for the association of each demand index with LPP difference wave amplitude and with probability of belonging to cluster drug > pleasant in separate models.
Results: Positive associations (posterior probabilities > 75%) were found between LPP difference wave amplitude and most demand indices (Q0, Omax, essential value). There was moderate evidence for an association between probability of membership in drug > pleasant cluster and Q0 (posterior probability=79%), where a 1%-increase in probability was associated with a 0.05%-increase in Q0.

Conclusions: To our knowledge, this is the first study to propose a positive association between the LPP and drug demand among individuals with CUD. Overall, our results suggest that individuals who attach greater relevance to cocaine-drug cues also exhibit greater valuation of cocaine reward.
Financial Support: This work was supported by NIDA F32DA048542 (HEW) and R01DA039125 (JMS).

AT-RISK DRINKING, OPERANT DEMAND, AND CROSS-COMMODITY DISCOUNTING AS PREDICTORS OF DRUNK DRIVING IN UNDERAGE COLLEGE WOMEN

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Drug Category Alcohol
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: The first aim of this investigation was to examine the extent to which at-risk drinking, operant demand for alcohol, and single- and cross-commodity discounting of money and alcohol predict adverse consequences of past-month drinking in underage college women. The second aim was to determine whether these clinical and behavioral economic measures could significantly predict the odds of past-month drunk driving, a serious public health concern due to the increasing prevalence of heavy episodic drinking among women in their first 1 – 2 years of college.
Methods: Seventy-two undergraduate women (aged 18 – 20 years) participated in this study. We assessed the number of hypothetical alcoholic drinks participants would consume across a range of monetary price points using the Alcohol Purchase Task. Participants also completed single- and cross-commodity discounting assessments for money and alcoholic drinks. Clinical measures of at-risk drinking included the consumption factor of the Alcohol Use Disorder Identification Test (AUDIT-C) and the Brief Young Adult Alcohol Consequences Questionnaire (B-YAACQ). The B-YAACQ involves 24 binary (yes/no) responses to statements about alcohol consumption and served as our measure of past-month drunk driving in addition to providing a total score. Alcohol demand was estimated using non-linear modeling and past-month drunk driving using hierarchical logistic regression.
Results: Underage college women with higher scores on the AUDIT-C (odds ratio [OR] = 1.67, $p = .02$), greater amplitude of demand (OR = 2.81, $p = .01$), and greater discounting on the alcohol now | money later task (i.e., choosing immediate alcohol instead of twice the equivalent in delayed money; OR = 2.56, $p = .02$) were significantly more likely to report past-month drunk driving.
Conclusions: We contend that operant demand along with single- and cross-commodity discounting can be viewed as intersecting measures of reinforcer value with clinical relevance to college women.
Financial Support: National Institute on Drug Abuse of the National Institutes of Health: T32 DA07209

SELF-REPORTED ANHEDONIA AND CRACK COCAINE DEMAND

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Drug Category Stimulants
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Individuals with cocaine use disorder (CUD) often overvalue drug rewards while undervaluing other reinforcers. This reinforcer pathology can be measured via cocaine demand and anhedonia assessments. Interestingly, no studies have investigated their relationship and shared impact on reinforcer pathology. Here, we examined the relationships between anhedonia, demand, and cocaine use severity, and between anhedonia and five indices of cocaine demand (Q0, Omax, Pmax, essential value (ev), breakpoint).
Methods: Participants (N=116), treatment-seeking males and females with CUD, completed baseline measures of cocaine demand, anhedonia, and self-report measures of cocaine use severity (30-day and lifetime use and amount spent).
Results: Correlations indicated significant associations between demand and lifetime use (Q0: $r = 0.23$, $p = 0.01$), 30-day use (Q0: $r = 0.19$, $p < 0.05$; ev: $r = 0.24$, $p < 0.01$), lifetime amount spent (Q0: $r = 0.28$, $p < 0.01$), and 30-day amount spent (Q0: $r = 0.20$, $p = 0.03$; ev: $r = 0.27$, $p < 0.01$), but not between anhedonia

and any measures of cocaine use severity. Regressions assessed if either construct (demand, anhedonia) captured separate variance in cocaine use severity. Anhedonia (β = -0.11, t = -2.03, p = 0.04) significantly predicted 30-day amount spent, but demand did not. Linear regressions suggested a significant relationship between anhedonia and breakpoint (p = 0.02), but no other demand indices.
Conclusions: Overall, demand was related to cocaine use severity. We did not observe consistent associations between anhedonia and cocaine demand except for breakpoint, suggesting they account for unique aspects of cocaine reinforcer pathology. As both anhedonia and demand have individually been associated with cocaine treatment outcomes, assessing both may provide improved predictive utility and help identify individuals with greater treatment need.
Financial Support: This research was supported by a grant from the National Institute on Drug Abuse to Dr. Joy M. Schmitz (DA039125).

ORAL COMMUNICATION: UNIQUE CHALLENGES FOR SUDS IN RURAL ENVIRONMENTS SUCCESSFUL IMPLEMENTATION OF SUBSTANCE USE SCREENING IN RURAL FEDERALLY-QUALIFIED HEALTH CENTERS IDENTIFIED HIGH RATES OF UNHEALTHY ALCOHOL, CANNABIS, AND TOBACCO USE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Screening for substance use in rural primary care clinics faces unique challenges due to limited resources, high patient volumes, and multiple demands on providers. To explore the potential for electronic health record (EHR)-integrated screening, we conducted an implementation feasibility study with a rural federally-qualified health center (FQHC) in Maine. This was an ancillary study to a NIDA Clinical Trials Network study of screening in urban clinics (CTN-0062).
Methods: Researchers worked with stakeholders from 3 FQHC clinics to define and implement their optimal screening approach. Clinics used the TAPS Tool, completed on tablets in the waiting room, and results were immediately recorded in the EHR. Adults presenting for annual preventive care visits were eligible for screening. Data were collected between 11/1/2018-5/5/2020, and analyzed for the first 12 months following implementation at each clinic to assess screening rates and prevalence of reported unhealthy substance use.
Results: Screening was completed by 3,749 patients, representing 93.4% of those eligible and 18.4% of all adult patients presenting for primary care visits. In 92.9% of cases, screening was self-administered. Current unhealthy substance use (TAPS score 1+ for at least one substance) was identified in 1,219 patients (32.5% of those screened): 508 (13.6%) had unhealthy use of tobacco, 1064 (28.4%) alcohol, 383 (10.2%) cannabis, 11 (0.3%) illicit drugs, and 18 (0.5%) non-medical use of prescription drugs.
Conclusions: Self-administered EHR-integrated screening was feasible to implement and detected substantial alcohol, cannabis, and tobacco use in rural FQHC clinics. Rates of drug use (including cannabis) identified through screening were higher (10% vs. 0.3-1.0%) than in the parent study, possibly because the TAPS allows patients to report cannabis separately from other drugs in a cannabis-legal state. Future work may broaden the reach of screening by offering it at routine visits rather than restricting to annual preventive care, within these and other rural clinics.
Financial Support: Supported by National Institute on Drug Abuse cooperative awards: UG1DA013035 (PIs John Rotrosen, Edward Nunes) and UG1DA040309 (PI Lisa Marsch) and by National Institute on Drug Abuse, National Institutes of Health, Department of Health and Human Services, Contract No. HHSN271201400028C / N01DA-14-2237 and Contract No. 75N95019D00013 / N01DA-19-2250

MHEALTH INTERVENTION FOR IMPROVING HIV, HEPATITIS C, AND OVERDOSE KNOWLEDGE AMONG RURAL ADULTS WITH OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: We previously demonstrated the initial effectiveness of a single-visit mobile health (mHealth) educational intervention for improving HIV and HCV related knowledge in a 12-week pilot study evaluating Interim Buprenorphine Treatment (IBT) for opioid use disorder (OUD) (Ochalek et al., 2018; Sigmon et al., 2016). We report here on a recently-completed trial which sought to extend those initial findings in several ways by including an additional module focused on overdose (OD) prevention, a longer study duration, and individuals residing in rural geographic areas.
Methods: Participants were 25 rural adults enrolled in a 24-week trial evaluating the efficacy of IBT for reducing illicit opioid use during treatment delays. Participants completed iPad-delivered baseline assessments of HIV, HCV, and OD knowledge with corrective feedback. They then completed interactive educational modules in these three content areas, followed by an immediate post-intervention knowledge assessment. HIV, HCV and OD knowledge were evaluated again at Weeks 4, 12 and 24 to assess for evidence of sustained improvements.
Results: Participants answered 62%, 52%, and 73% of items correctly on the baseline HIV, HCV, and OD knowledge assessments, respectively; this increased to 81%, 80%, and 93% immediately following the mHealth intervention (p's<0.001). Improvements persisted with scores at Week 4, 12, and 24 significantly greater than baseline across the three content areas (p's<0.001).
Conclusions: These data provide additional evidence that a single-visit mHealth intervention significantly improves HIV and HCV knowledge among individuals with OUD, as well as new evidence of sustained effects through 6 months and extension to a rural patient population. This is also the first demonstration of significant and sustained improvements in OD-related knowledge among patients receiving IBT. Additional data will be presented from individual item analysis. Taken together, brief, single-visit mHealth platforms may hold promise for improving harm-related knowledge among patients in resource-constrained rural settings.
Financial Support: This work was supported by NIDA (R01DA042790, T32 DA007242).

PROFILE DIFFERENCES IN MEDICATION ASSISTED OPIOID TREATMENT IN RURAL PRACTICES

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid use disorder (OUD) is a chronic illness that burdens multiple aspects of life. Medication assisted opioid treatment (MAOT) reduces the severity and mortality of OUD, improves treatment retention, and prevents sexually transmitted infections. Despite its effectiveness, the US has the highest estimated prevalence of OUD worldwide. Given the barriers to MAOT, rural and minority populations may be more impacted. The objective of this study was to identify clinical and profile differences among individuals initiating MAOT with methadone versus suboxone in rural and remote areas of the US.
Methods: This study was conducted in collaboration with the Oregon Rehabilitation and Treatment Centers (ORTC). Data was extracted from four rural ORTC clinics providing MAOT in 2020.
Results: Of the 546 participants, the majority were White (n=492, 90.1%). The mean age was 36.9 years old (SD=10.9), the majority were male (n=306, 56.3%) and predominantly heterosexual (n=512, 94.8%). Over 70% of participants (n=422) received methadone compared to 29.4% (n=124) suboxone. Participants receiving methadone were more likely to have positive urinalysis results for opiates (X2= 8.5, p=0.01), methamphetamine (X2= 6.1, p=0.01) and cocaine (X2= 4.5, p=0.03) when compared to suboxone. Likewise, the proportion of participants with a more severe OUD diagnosis, or who were experiencing homelessness was significantly higher among those enrolled in methadone (X2 = 4.5, p=0.03; X2= 6.3, p=0.01).

Conclusions: Our findings suggest that participants enrolled in methadone treatment present a more severe substance use disorder and experience more homelessness when compared to participants enrolled in suboxone treatment in rural settings.

METHAMPHETAMINE USE AND UTILIZATION OF MEDICATIONS FOR OPIOID USE DISORDER AMONG RURAL-AREA PERSONS WHO USE DRUGS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Methamphetamine (MA) use is increasingly common, particularly in rural areas, and often co-occurs with opioid use. The study aims were to evaluate whether MA use was associated with utilization of medications for opioid use disorder (MOUD) in rural communities across the U.S.
Methods: This analysis utilized cross-sectional survey data from the Rural Opioid Initiative (ROI), a NIDA-funded consortium of 8 studies spanning 10 states and 65 rural counties. Persons who reported use of opioids and/or injection drug use were recruited between 1/2018 and 3/2020. Analyses were restricted to participants with recent (past 30-day) use of opioids who also had data on recent MA use. Using multilevel logistic regression and Poisson generalized linear regression accounting for sites and adjusted for age, sex, and race, we examined three outcomes: 1) recent treatment with MOUD (buprenorphine and/or methadone), 2) days of MOUD treatment in past 6 months, and 3) inability to access MOUD in the past 6 months.
Results: Among 2,533 participants with opioid use, 1,901 (75%) also reported recent MA use. Compared to those without MA use, MA users were younger, more likely to have injected drugs and been homeless, and less likely to have health insurance. In adjusted multilevel models, recent MA use was associated with lower relative odds for recent methadone treatment (aOR=0.70; 95% CI: 0.49-0.998). Participants with MA use also reported less treatment days with buprenorphine (aIRR=0.90; 0.88-0.93) and methadone (aIRR=0.76; 0.58-1.01) although the latter did not meet thresholds for statistical significance. There was no association with MA use and recent buprenorphine treatment (aOR=0.97; 0.72, 1.31), nor perceived inability to access either buprenorphine (aOR=1.18; 0.90-1.57) or methadone (aOR=1.07; 0.76-1.53) in the past 6 months.
Conclusions: MA use is common among persons who use opioids in rural areas of the U.S., and it appears to adversely impact MOUD utilization.
Financial Support: Rural Opioid Initiative (ROI), a multi-site study with a common protocol which was developed collaboratively by investigators at eight research institutions and at the National Institute of Drug Abuse (NIDA), the Appalachian Regional Commission (ARC), the Centers for Disease Control and Prevention (CDC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). Research presented is the result of secondary data harmonization and analysis and was supported by grant U24DA048538 from NIDA. Primary data collection was supported by grants UG3DA044829/UH3DA044829, UG3DA044798/UH3DA044798, UG3DA044830/UH3DA044830, UG3DA044823/UH3DA044823, UH3DA044822/UH3DA044822, UG3DA044831/UH3DA044831, UG3DA044825, UG3DA044826/UH3DA044826, and U24DA044801 co-funded by NIDA, ARC, CDC, and SAMHSA.

SUNDAY, JUNE 12, 2022

POSTER SESSION 1

S1. Association of Phosphotidylethanol (PEth) Levels With Severity of Dependence in Alcohol Dependent Patients- A Cross-Sectional Study

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Phosphotidylethanol (PEth), a direct biomarker for alcohol can be measured in whole blood for up to 4 weeks depending on the amount of alcohol consumed. It is well suited to monitor abstinence, drinking behavior and to identify relapse because it can detect both chronic and occasional alcohol consumption. The current study aimed to assess the association of PEth levels with the severity of dependence in alcohol-dependent patients.
Methods: A cross-sectional study was conducted in an outpatient setting with 30 adult males, first-time treatment seeking patients of dependence on alcohol (based on ICD 10 criteria). A urine cassette test was done to rule out illicit opioid use and benzodiazepine use in the past 3 days. Alcohol Use Disorder Identification Test (AUDIT) was used to screen patients for harmful alcohol use and Severity of Alcohol Dependence Questionnaire (SADQ) was used for assessing the severity of dependence. PEth estimation in whole blood sample (2ml) was done by LC-QTOF-Mass -spectrometry. Analysis was done using SPSS version 26.
Results: PEth levels (Median= 783.5 ng/ml; Range: 21- 1998 ng/ml) were positively correlated with total scores of SADQ (r= 0.33) and AUDIT (r= 0.28) whereas age (Mean= 36.2 +/- 9.4 yrs) was negatively correlated (r= -0.352) with PEth levels. The majority (64%) of the patients had binge drinking pattern.
Conclusions: Higher PEth concentrations indicated excessive alcohol consumption which could be due to the treatment-seeking population at a tertiary centre when compared to the general population setting. To the best of our knowledge, this is the first study of its kind from India. A future study with larger sample size is needed in designing personalized treatment which will augment the long-term recovery in patients.
Financial Support: National Drug Dependence Treatment Centre, AIIMS, New Delhi, India

S2. Associations Among Perceived Risk, Age of Marijuana and Alcohol Onset, and DSM-IV Alcohol Use Disorder and Marijuana Use Disorder in a Sexual Minority Population

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Lesbian, gay, and bisexual individuals exhibit elevated rates of alcohol use disorder (AUD) and marijuana use disorder (MUD) compared to heterosexual peers (Schuler and Collins, 2019). Perceived risk of a substance use and earlier age of onset are associated with AUD and MUD (Okaneku et al., 2015). This study examined LGB substance use through associations among perceived risk of alcohol and MJ, age of onset for alcohol and MJ, and AUD/MUD.
Methods: The 2019 National Survey of Drug Use and Health included a sample of US adult (18+) LGB individuals (n = 3,038) and assessed age, biological sex, English fluency, education, race/ethnicity, and family income, perceived risk of alcohol and MJ, age of onset for alcohol and MJ, and AUD/MUD. Six models with two-way interactions (age of onset X sexual identity, perceived risk X sexual identity, age of onset X perceived risk) were conducted using logistic regression to determine associations with AUD/MUD in LGB individuals after controlling for demographics.

Results: The main effects of age of onset (MUD: OR= 0.02, p<0.001; AUD: OR = 0.01, p<0.001), perceived risk (MUD: OR=0.24, p<0.001; AUD: OR=0.07, p<0.0001), and sexual identity (MUD: OR= 0.05, p<0.001; AUD: OR=0.05, p<0.001) were significantly associated with greater odds of AUD and MUD. The interaction between age of onset and sexual identity was significantly associated with greater odds of AUD (OR=0.02, p<0.05) but not MUD. No other interactions were significantly associated with AUD or MUD.
Conclusions: Findings suggest age of onset of alcohol moderated the relationship between sexual identity and AUD but not MUD. Results indicated that age of onset of alcohol within the context of sexual identity might be prescient in understanding the etiology of AUD. Further research is needed to understand the role of age of onset of MJ in development of MUD among LGB individuals.

S3. Driving Under the Influence of Alcohol, Marijuana, and Select Illegal Drugs by Sexual Identity and Gender

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Drug Category Alcohol
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Aim: Compare the prevalence of driving under the influence (DUI) of alcohol, marijuana, and other drugs by gender, race/ethnicity, and sexual identity among adults living in the US.
Methods: Methods: Data were pooled for adults ages 18+ in the 2016-2019 National Survey on Drug Use and Health (n=170,944; analyzed in 2021). Survey-weighted logistic regression models, stratified by gender and race/ethnicity, examined associations between sexual identity and past-year (1) DUI involving alcohol among adults who used alcohol, (2) DUI involving marijuana among adults who used marijuana, and (3) any DUI involving alcohol, marijuana, or select illegal drugs among adults who used any of these substances.
Results: Results: Combined DUI prevalence (i.e., DUI involving alcohol, marijuana, or select illegal drugs) varied by sexual identity (men: heterosexual, 11.3%; gay, 18.7%; bisexual, 19.8%; women: heterosexual, 11.3%; lesbian, 19.0%; bisexual, 23.5%). In general, relative to heterosexuals of the same gender and race/ethnicity, sexual minority adults had higher odds of DUI across all categories. For example, bisexual men reported higher odds of DUI involving alcohol than heterosexual men (White, AOR=1.42, 95% CI=1.42, 1.43; Black, AOR=1.43, 95% CI=1.40, 1.45; Hispanic, AOR=1.33, 95% CI=1.32, 1.34). Bisexual women reported higher odds of DUI involving alcohol than heterosexual women (White, AOR=1.19, 95% CI=1.19, 1.20; Black, AOR=1.22, 95% CI=1.20, 1.23; Hispanic, AOR=1.91, 95% CI=1.89, 1.92). Hispanic lesbian women reported the highest odds of DUI involving alcohol (AOR=2.99, 95% CI=2.96, 3.03), marijuana (AOR=1.78, 95% CI=1.76, 1.81), and alcohol, marijuana, or select illegal drugs (AOR=2.85, 95% CI=2.83, 2.88).
Conclusions: Conclusions: Sexual minority adults consistently had a higher prevalence of DUI than their heterosexual counterparts. The most significant differences in DUI prevalence were observed between Hispanic lesbian and heterosexual women. These findings highlight the need for research that identifies risk factors that influence risk for DUI among gay, lesbian, and bisexual adults.
Financial Support: T32DA031099 (Hasin) and R01DA037866 (Martins)

S4. Longitudinal Patterns and Demographic, Family History, and Psychopathology Predictors of Substance Use Initiation in the ABCD Study Cohort

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Drug Category Alcohol
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: The Adolescent Brain Cognitive Development (ABCD) Study is a multi-site study that aims to examine risk and protective factors linked with substance use (SU) initiation and escalation. Previously

reported baseline ABCD patterns identified the majority of SU as alcohol sipping and minimal full SU. Here, we highlight early adolescent longitudinal SU methods, patterns, and multivariate onset analyses.
Methods: Data from the ABCD Study Annual Release 4.0 was used, representing a diverse cohort of n=10,414 youth (ages 9-14) across 21 catchment sites across the United States (includes half of YR3 follow-up; n=6,251). Participants are given a standard battery of SU surveys, as part of the study battery (Lifetime Use Interview, Timeline Followback, and iSay Sip Inventory.) Generalized estimating logistic equations were used to investigate SU trying (>sipping/puffing) and full SU (>1 standard use)through standardized odds ratios (OR), with demographic, family history, and psychopathology predictors.
Results: Alcohol sipping remains the most popular SU (baseline 23%), with yearly increases in new at each wave (9.7% YR1-12.8% YR3). Although the cohort remains primarily SU-naïve, longitudinal increases (B-YR3) in using nicotine (0.7%-2.2%), cannabis (0.1%-0.9%), or any SU (0.9%-2.3%) were observed. Models predicting SU trying observed significant demographic predictors (i.e., age, sex, race, ethnicity, household income, marital status, and parental education). Predicting full SU revealed a higher likelihood of SU for males (OR=1.5), youth with a parental history of SU problems (OR=1.4), and externalizing symptoms (OR=1.1), and a lower likelihood for those with parents who are married (OR=0.6).
Conclusions: SU is escalating across time within the ABCD cohort and mirrors prevalence rates observed in other epidemiological studies examining early adolescent SU. Demographic variables, familial history of use, and psychopathology continue to be significant predictors of SU status and should continue to be assessed in analyses of onset and escalating SU trajectories in the cohort.
Financial Support: U01DAO41025 PI: Lisdahl, K.M.; F31DA054761 PI: Sullivan, R.M.

S5. Sex-Specific Associations in Patients With Alcohol Use Disorder Admitted for Hospital Detoxification

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Drug Category Alcohol
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Sex-specific associations among patients with alcohol use disorder (AUD) have received little attention in the literature.
Methods: We studied patients admitted for treatment of AUD between 2013 and 2021 at two hospitals in Barcelona. Information around alcohol use, presence of hypertension, diabetes and dyslipidemia were gathered through interview and medical chart review. We performed analyses to assess if female sex was associated with the presence of comorbidities or with values markers of monocyte activation (sCD163 and sCD14), inflammation (interleukin (IL)-6 and IL-10), and microbial translocation (lipopolysaccharide (LPS) and LPS binding protein).
Results: A total of 465 patients (23% women) were included. Median age was 50 years [Interquartile range (IQR):43-57], median alcohol intake before admission was 150 grams/ day [IQR: 100-224] and median duration of AUD was 20 years [IQR: 10-28]. Median body mass index was 25.6 [IQR: 22.9-29.4]. The prevalence of hypertension, diabetes mellitus and dyslipidemia was 32.6%, 12.4% and 49.3%, respectively. Median values of sCD163, sCD14, IL-6, IL-10, LPS and LPS binding protein were 734 ng/ mL, 1.72 x 106 pg/ mL, 3.3 pg/ mL, 0.56 pg/ mL, 846 pg/ mL and 26 pg/ mL
Women had lower levels of alcohol consumption (134 vs. 177 gr/day, $p<0.01$), shorter length of AUD (15 vs. 21 years, $p<0.01$), lower prevalence of diabetes (6% vs. 14.5%, $p=0.01$) and lower prevalence of sCD163 and IL-10 in the highest quartile (16% vs. 17%, $p=0.02$ and 17% vs. 26% $p=0.04$; respectively). No other sex-associated differences were found.
Conclusions: In this predominantly male case-series, women had a lower alcohol intake, a shorter duration of AUD, had a lower prevalence of diabetes and lower levels of sCD163 and IL-10. Despite that, they needed admission because of their severity of AUD and prior unsuccessful attempts of ambulatory detoxification. Studies with a focus on women with AUD are warranted.
Financial Support: This research was partially funded by the Ministry of Economy and Competitiveness, Institute of Health Carlos III (RETICS RD16/0017/0003, Programa Juan Rodes JR20/00016, Programa Sara Borrell CD19/00019, grant nos. PI17/00174 and PI20/00883, and Redes de Investigación Cooperativa

Orientadas al Resultado en Salud RD21/0009/0004 202), European Fund for Regional Development (FEDER), Ministry of Health, Social Services and Equality, National Plan on Drugs, Spain (grant nos. 2018/020 and 2020/024), and Consolidated Research Group (2017-SGR-316), Autonomous Government of Catalonia, Spain.

*S6. The Effect of Comorbid Alcohol Use Disorder on Major Depressive Disorder Treatment Outcomes: A STAR*D Analysis*

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Drug Category Alcohol
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Guidance on depression treatment in those with comorbid Major Depressive Disorder (MDD) and Alcohol Use Disorder (AUD) is lacking. We performed a secondary analysis on the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, a multi-site, real-world effectiveness trial following outpatients with MDD through 4 sequential antidepressant treatment levels (or until remission), examining the effect of comorbid AUD on depression outcomes.
Methods: AUD was identified at baseline through the Psychiatric Diagnostic Screening Questionnaire. Treatment response was defined as ≥50% score reduction on the Hamilton Rating Scale for Depression-17 (HRSD-17) and remission as a score ≤7. Logistic regression analysis was performed to evaluate remission/response predictors in the total STAR*D sample and for the AUD-comorbidity interaction. Demographic/clinical and medication factors were included as covariates across levels 1-2 and medications only in levels 3-4 as permitted by sample size. In total, 2826 MDD patients and 864 with comorbid AUD were included in the analysis.
Results: Comorbid AUD was not a significant predictor of response/remission across levels. Higher baseline HRSD-17 score associated with overall lower odds of remission in treatment level 1 (OR=0.93, $p<0.001$) and 2 (OR=0.95, $p<0.001$), with no significant interaction when considering comorbid AUD. Higher baseline suicidality had overall lower odds of remission in treatment level 1 (OR=0.82, $p<0.001$) and 2 (OR=0.1, $p<0.001$), but for those with comorbid AUD, suicidality associated with increased odds of level 1 remission (OR=1.30, p=0.012). In comorbid AUD, venlafaxine was associated with lower odds of remission (OR=0.13, p=0.013) and response (OR=0.12, p=0.006) and bupropion with lower odds of response (OR=0.22, p=0.024).
Conclusions: Comorbid AUD may not influence antidepressant effectiveness over multiple treatment trials. In those with comorbid AUD, higher baseline suicidality and depression severity was not associated with worse outcomes, and after an initial failed treatment trial, using venlafaxine or bupropion may be less effective than other treatments.
Financial Support: Supported by the Centre for Addiction and Mental Health (CAMH) Discovery Fund and the Research in Addiction Medicine Scholars (RAMS) Program, R25DA033211 from the National Institute on Drug Abuse.

S7. Alcohol Use Disorder is Associated With Lower Receipt of Direct-Acting Antiviral Hepatitis C Treatment: A Cohort Study

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Drug Category Alcohol
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Direct-acting antivirals (DAA) for hepatitis C virus infection (HCV) are effective in those with current or past alcohol use disorder (AUD), a group with a high prevalence of liver disease. Patients with AUD may be less likely to receive DAAs despite guideline recommendations. We assessed the association between AUD and DAA receipt among patients with HCV at the Veterans Health Administration (VHA).
Methods: This retrospective study included patients with HCV, born between 1945-1965, and documented Alcohol Use Disorder Identification Test for Consumption screen. Cohort entry was the first VHA visit in 2014-2017, on or after HCV diagnosis. Alcohol use categories were: current AUD by ICD 9/10, abstinent with AUD history, at-risk drinking, lower-risk drinking, abstinent without AUD history. The association between alcohol use and DAA receipt in the first year after entry was estimated using Cox regression stratified by calendar year.
Results: Among 133,753 patients, mean age at entry was 61 years (SD 4.5). Most were male (97%) and white (55%). Alcohol use was: current AUD (38%), abstinent with AUD history (12%), at-risk drinking (6%), lower-risk drinking (14%), abstinent without AUD history (30%). Receipt of DAAs within one year was 7%, 33%, 53%, and 56% in 2014, 2015, 2016, and 2017, respectively. For patients entering in 2014, those with current AUD (HR 0.69, 95% CI 0.64-0.75) or abstinent with AUD history (HR 0.90, 95% CI 0.82-0.99) were less likely to receive DAAs than those with lower-risk drinking. For those entering 2015-2017, current AUD (HR 0.73, 95% CI 0.68-0.78) and abstinent with AUD history (HR 0.76, 95% CI 0.67-0.86) were also associated with lower DAA receipt.
Conclusions: Individuals with AUD regardless of current self-reported alcohol use are persistently less likely to receive DAAs. Improved DAA access for persons with AUD is needed.
Financial Support: The COMpAAAS/Veterans Aging Cohort Study, a CHAART Cooperative Agreement, is supported by the National Institutes of Health: National Institute on Alcohol Abuse and Alcoholism (U24-AA020794, U01-AA020790, U01-AA020795, U01-AA020799; U10 AA013566-completed) and in kind by the US Department of Veterans Affairs.

S8. Harms From Other's Drinking: Risk Factors and Help-Seeking Behaviors in Taiwan

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Drug Category Alcohol
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The harms associated with alcohol drinking may exceed drinkers themselves. To better address alcohol burden in the community, the present study is aimed to evaluate the prevalence of alcohol harms from others, potential effects with quality of life, and help-seeking behaviors, with stratification by gender.
Methods: Building upon the 2018 National Survey of Substance Use in Taiwan, we ascertained 12,928 adults aged 25~64 year-old with national representativeness (male: 6582; female: 6341). Information concerning sociodemographic status, alcohol drinking, harms from others' drinking (i.e., physical, psychological, and financial) and help-seeking behaviors, and quality of life (assessed by EQ-5D questionnaire) were assessed by computer-assisted self-interview. Complex survey analyses were used to estimate the prevalence and association.
Results: Nearly 5% of men and 4% of women had experienced any alcohol harms from others, and the most common form was psychological harms (4.4% and 3.5%); only 19.8% of harmed men and 42.2% harmed women sough for help. Younger age and divorce/widowhood-related increased odds of having alcohol harms from others were generally greater in men; however, heavy episodic drinking-related increased odds was especially prominent in women (Odds Ratio=10.0 vs 3.3 in men). Having harms from other's drinking appeared to be one of the strongest predictors for lowered quality of life in both genders (β =-.12~-0.14).

Among those experienced harms from other's drinking, female gender and living alone may increase the odds of help-seeking behaviors by 210% and 159%, respectively.
Conclusions: The vulnerability toward alcohol harms from others was greatly shaped by disadvantaged social fabric and one's drinking behaviors, and such risks evidently vary by gender. Prevention policy and program addressing alcohol harms in community should be developed and implemented while integrating gender and contextual relevance.
Financial Support: Ministry of Science and Technology (110WFA2210076)

S9. High-Throughput LC-QTOF-Mass Method for Determination of Phosphatidylethanol (PEth) in Whole Blood for Monitoring Alcohol Consumption in Alcohol Dependent Subjects

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Phosphatidylethanols (PEths) are specific, direct alcohol biomarkers that can be determined in human blood to distinguish between heavy and social drinking or to confirm alcohol abstinence. The study aimed to develop a high throughput and sensitive LC-QTOF Mass method for detection of PEth 16:0/18:1 in whole blood for monitoring alcohol consumption in alcohol-dependent subjects.
Methods: Phosphatidylethanols were extracted from (100µL) whole blood by addition of (100µL) PEth-d5 internal standard (300ng/mL), and 800µL of acetonitrile and 2-propanol (40:60), vortexed and centrifuged for 10 minutes at 14,000 rpm. The supernatant was dried under a stream of nitrogen, reconstituted (300 µL) of acetonitrile: methanol:2-propanol: water (30:10:30: 30), injected into LC system coupled to the AB Sciex Triple TOF 5600+ System. Chromatographic separation was achieved with the Kinetex® C-18 column (2.6 µm 30 x 2.1mm i.d Phenomenex). A mixture of methanol and 5mM Ammonium acetate buffer was used as a mobile phase. The method was validated for system suitability, linearity, accuracy, precision, detection, and quantification limits.
Results: Total run time for the assay is 6 mins and retention time of PEth is 4.0 mins. The m/z for precursor ion is 701. 5 and product ions are 281.2 and 255.2. The calibration curve was linear in the range 5 to 2000 ng/mL with a correlation coefficient higher than 0.993. Precision and accuracy were acceptable and the recovery was 80%. The limit of quantification (LOQ) was 5ng/ml. This method was successfully applied to the whole blood of alcohol-dependent subjects undergoing treatment at our Centre.
Conclusions: The current LC-QTOF-Mass spectrometry method is simple, sensitive, and precise. Accurate, reproducible results were achieved with a simple protein precipitation procedure. It is fast, economical and can be used for monitoring alcohol consumption among alcohol-dependent subjects in clinical settings.
Financial Support: Supported by National Drug Dependence Treatment Centre, AIIMS, New Delhi, India.

S10. Negative Mood Symptoms and Alcohol Use in Firefighters: The Moderating Effects of Drinking Motives

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Firefighters are an understudied population with high rates of alcohol use and negative emotional states partly related to chronic exposure to stress and potentially traumatic events. Individuals with heightened emotional distress who use alcohol to cope (i.e. reduce negative emotions) report using alcohol at greater rates. Notably, there has been comparably little attention to the role of other drinking motives, such as approach-oriented motives (i.e., to enhance social experiences [social] and to boost mood states [enhancement]), among populations at an increased risk for alcohol use. Here, we examined the moderating role of four common drinking motives (i.e., coping, conformity, social, and enhancement motives) in the

association between negative mood and alcohol use severity among firefighters. We hypothesized that firefighters with heightened negative mood symptoms and greater coping motives would report more severe alcohol use.
Methods: Current full-time male and female firefighters (N = 685) at a large urban fire department participated in a voluntary online survey on stress and health-related behaviors. Four linear regressions were fit to investigate coping, conformity, social and enhancement drinking motives as potential moderators of the association between negative mood and alcohol use severity.
Results: The main effects of negative mood and each drinking motive were significantly associated with alcohol use severity. However, only the interactive effects of negative mood with enhancement motives (B = .01, SE = .001, t(678) = 2.68, p = .008) and social motives (B = .01, SE = .001, t(678) = 3.3, p = .001) were significantly related to alcohol use severity.
Conclusions: Results suggest that when negative mood is experienced alongside approach-oriented drinking motives (social or enhancement), firefighters may engage in more severe alcohol use. This study suggests that drinking for social rewards or to enhance mood may be clinically relevant for understanding alcohol use among firefighters who experience negative mood.

S11. Perceived Stigma, Self Stigma and Barriers to Treatment in Alcohol Dependent Individuals

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Drug Category Alcohol
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of the present study was to study barriers of treatment seeking and assess self and perceived stigma in alcohol dependent male patients in rural population of India
Methods: An observational study was conducted at a private de-addiction center in India. Male patients who were more than 18 years old, alcohol dependent with more than seven days of admission (not currently in withdrawal) were included in the study
Results: The mean age of the sample was 29.1 (7.8) years and age of onset of alcohol use was 18.5 (3.3) years. The mean quantity of alcohol used per day was around 550 millilitres of IMFL per day. The mean number of previous abstinent attempt were two. The most common barrier to treatment was financial (poor affordability). Not serious enough to change and being afraid of what others might think (stigma) were other common barriers. The mean value of perceived stigma was 21.9 (2.3). No co-relation was observed between stigma (both perceived and self stigma) and age of onset and quantity of alcohol consumed
Conclusions: These barriers and stigma needs to be addressed to improve treatment seeking and reduce relapse in our population

S12. Races, ACEs, and Places: The Interaction Effects of Race, Childhood Adversity, and Neighborhood Disadvantage on Alcohol Use Disorder

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Drug Category Alcohol
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Alcohol use disorder (AUD) is a significant public health concern facing adolescents in the United States. Justice-involved adolescents (JIA) have a higher risk for AUD and may suffer harsher consequences than adolescents in the general population, such as addiction, recidivism, and early death. Adverse childhood experiences (ACEs) and neighborhood disadvantage have been linked to AUD, and may be key factors underlying racial differences in risk for AUD. However, current research has not explored whether ACEs and neighborhood disadvantage are key mechanisms behind racial disparities in AUD among JIA.
Methods: Multivariate logistic regression was employed to analyze longitudinal data on 36,000 adolescents from the Florida Department of Juvenile Justice (FLDJJ). This sample represents adolescents arrested in Florida between 2016 and 2018, completed the full Positive Achievement Change Tool assessment during

the enrollment process and reassessed every three to six months, reached the age of 18 by 2018, and have data on AUD. Childhood adversity was operationalized by a 10-item interval level index based on the original ACEs instrument. Neighborhood disadvantage was defined by the Child Opportunity Index (COI) using census tract ID. Marginal odds were estimated to test the interaction effects between race, ACEs, and COI on AUD. The study controls for known predictors such as age, household income, and family support.
Results: Preliminary results indicate that ACEs were associated with a 108% increased likelihood of AUD among Black JIA and neighborhood disadvantage were associated with a 53% increase in the odds of AUD among Latinx JIA compared to White JIA.
Conclusions: The results support the development of programs that target childhood adversity and neighborhood disadvantage to eliminate or reduce these disparities. Data indicates that Black JIA may benefit from family-level interventions while Latinx JIA may benefit from community- level interventions.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

S13. Correlates and Consequences of Anxiety and Depressive Symptom Trajectories During Early Treatment for Alcohol Use

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Drug Category Alcohol
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: The current study sought to (1) identify anxiety and depressive symptom trajectories during early recovery from alcohol use, (2) explore clinical correlates of trajectory membership, and (3) investigate whether trajectory membership predicts discharging against medical advice (AMA).
Methods: Respondents included individuals in treatment for alcohol use in addiction treatment facilities across the U.S. who presented with anxiety (N=6158, 56.7% Male, 82.5%White) and/or depressive (N=6209, 56.9% Male, 82.9% White) symptoms at intake. Growth mixture modeling was used to identify anxiety and depressive symptom trajectories. Multinomial logistic regression was used to examine whether clinical factors were associated with trajectory membership and whether trajectories were predictive of discharge AMA.
Results: Three anxiety symptom trajectories were identified: 1) Persistent Moderate Anxiety Symptoms, 2) Remitting Anxiety Symptoms, and 3) Mild Anxiety Symptoms. Compared to the Mild Anxiety Symptoms trajectory, the (a) Persistent Moderate Anxiety Symptoms trajectory was more likely to be female, younger, and endorse more non-heavy past month benzodiazepine and less non-heavy cannabis use, and (b) Remitting Moderate Anxiety Symptoms trajectory was more likely to report heavy past month cannabis use. The Mild Anxiety Symptoms trajectory was less likely to discharge AMA than the Persistent Moderate Anxiety Symptoms trajectory.
Three depression symptom trajectories were observed: 1) Persistent Moderate Depressive Symptoms, 2) Remitting Depressive Symptoms, and 3) Mild Depressive Symptoms. Relative to the Mild Depressive Symptoms Trajectory, individuals in the Persistent Moderate Depressive Symptoms trajectory were more likely to be female, younger, screen positive for anxiety symptoms, and less likely to use cannabis non-heavily in the past month. Individuals in the Mild Depressive Symptoms trajectory were less likely to discharge AMA than the Persistent Moderate Depressive Symptoms trajectory.
Conclusions: The current study highlights heterogeneity in anxiety and depressive symptom progression and potential targets for treatment among individuals in treatment for alcohol use.
Financial Support: U01HL150835

S14. Fine Particulate Matter Exposure in Neighborhood is Associated to Early Substance Use Initiation in Youth

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Drug Category Alcohol
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: Recent studies have demonstrated air pollution exposure as a detrimental neurotoxin and is associated with neurological damages to the brain and neurodevelopmental disorders. Some research has posited air pollutants to impact the developing brain via white matter microstructures as a mechanism for risk for negative health outcomes. Neurocognitive development, including white matter health, has important implications for substance use (SU) initiation, however few studies have investigated the association of air pollution exposure and SU in youth. The aim of this study is to investigate the relation among air pollution exposure and SU initiation (i.e. trying, sipping, puffing, etc. any drug) among young adolescents.
Methods: Using baseline data from the 2020 NDA 3.0 data release of the ABCDTM study, this study used geocoded particulate matter air pollution exposure (PM2.5) that were estimated using an ensemble-based model approach and matched to each individual's primary residential address collected at the baseline visit. A logistic regression model was used to examine the cross-sectional association of PM2.5 and the relation to any SU initiation in 9,250 9- and 10- year olds adjusting for various socio-demographic factors (i.e. sex, age, household income, parent education, and area deprivation index).
Results: It was found that greater air pollution exposure at baseline was associated with lower odds of SU initiation (b = -0.05; p = 0.0042; Odds Ratio = 0.949; 95% Confidence Interval = -0.089 - -0.017;) holding all other predictor variables constant.
Conclusions: Preliminary results demonstrate that living in neighborhoods with greater air pollution exposure was linked with less SU initiation among 9- and 10-year olds. Notably, these results are preliminary and primarily capture the onset of late childhood alcohol sipping, which is most often provided by the parents. Future directions will include a longitudinal analysis of air pollution and greater SU initiation into early adolescence.
Financial Support: Supported by the National Institutes of Health Grant: U01DA041025.

S15. Nicotine Does Not Speed the Development of Recovery-Like Behavior in a Rat Model of Alcohol Use and Recovery Following Chronic Ethanol Exposure

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Drug Category Alcohol
Topic Substance Use Disorder
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Maintaining new habits is critical to successful recovery from alcoholism and requires cognitive flexibility. However, chronic ethanol exposure decreases cognitive flexibility which may impede recovery. One potential mechanism for this decrement may be ethanol-induced hypofunction of the nicotinic acetylcholine system. Reversing this might improve cognitive flexibility and facilitate recovery. Previously, we established an operant rat model of recovery in which, stimuli that occasioned drinking become increasingly ineffective over sessions in which the rat engages in alternative behavior (food-maintained responding) instead of working for ethanol. Here, we explore whether nicotine exposure (0.1 mg/kg) prior to engaging in recovery-like behavior enhances this shift in discriminative control away from alcohol use toward recovery-like behavior.
Methods: Rats were exposed to 10 or 20 days of extra-session ethanol exposure or water using a post-prandial drinking procedure. During this time, rats also responded during daily operant sessions where contingencies were arranged such that rats were exposed to a stimulus (ETH) signaling ethanol was available and food was not. Then, rats received an injection of nicotine or vehicle 15 minutes prior to each daily recovery-like session in which a distinct stimulus signaled both food and ethanol were available. On selected days (0,1,2,4,8) after the recovery-like phase was initiated rats were exposed to ETH and food and ethanol responses were compared under extinction.

Results: Rats with extra-session ethanol drank more than those provided to water (4.1 vs 1.2 g/kg/d, t=4.5, df=6, p<0.01), and exhibited slower shifts in discriminative control over drinking. Contrary to our hypothesis, nicotine-exposed rats persisted in responding for ethanol longer both within and between test sessions than controls, suggesting nicotine further slowed shifts in discriminative control over drinking.
Conclusions: Enhancing nicotine signaling did not speed the shift in discriminative control over drinking under these experimental conditions. Experiments using additional nicotine and ethanol doses are planned.
Financial Support: Supported by AA025664

S16. Racial Differences in the Effects of Parent and Sibling Alcohol Misuse on the Odds of Alcohol Misuse Among Justice-Involved Adolescents

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Drug Category Alcohol
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: The juvenile justice system has become the de facto treatment center for alcohol misuse among adolescents, especially racial minorities. Justice-involved adolescents (JIA) have a high prevalence of family risk factors and endure worse health outcomes. Social learning theory posits that the etiology of substance misuse may be rooted in key social relationships, like parents and siblings. However, racial differences in the association between parents' and siblings' alcohol misuse and the odds of alcohol misuse among JIA have not been investigated.
Methods: Stratified logistic regression was employed to analyze a statewide representative sample of 65,248 JIA from the Florida Department of Juvenile Justice. Participants' alcohol misuse was measured via a binary variable self-reporting past 30-day alcohol misuse-related problems. Parent and sibling alcohol misuse was self-reported data of parents' and siblings' lifetime alcohol misuse-related problems.
Results: Compared to JIA who did not report parent or sibling alcohol misuse, sibling-only alcohol misuse was associated with 34% increased odds of JIA alcohol misuse while parent-only alcohol misuse was associated with 71% increased odds of JIA alcohol misuse. Parent and sibling alcohol misuse was associated with 61% increased odds of JIA alcohol misuse. Racial patterns emerged. Sibling alcohol misuse was associated with 53% increased odds for alcohol misuse among White and Latinx JIA, but was not associated with alcohol misuse for Black JIA. Parent-only alcohol misuse had a greater impact on Latinx JIA (95% increased odds) than White (77% increased odds) and Black JIA (61% increased odds). Both sibling and parent alcohol misuse had a greater impact among White JIA (205% increased odds) relative to Black (123% increased odds) and Latinx JIA (128% increased odds).
Conclusions: The results suggest that family-focused treatment programs may be effective for addressing alcohol misuse across all JIAs. Parenting programs may be particularly beneficial in reducing alcohol misuse for Latinx and Black JIA.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

S17. Racial Differences in the Relationship Between Treatment Completion and Optimism Among Opioid Users in the Juvenile Justice System

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Drug Category Alcohol
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Opioid deaths have dramatically increased among Black individuals, prompting a push for equitable access to treatment. The population of adolescents in the juvenile justice system are disproportionately Black and Latinx and have a higher risk for substance misuse relative to national samples of adolescents. Some scholars suggest that the primary culprit is structural racism, which modern treatment programs do not address. If the underlying impetus of opioid misuse for certain groups is rooted in their lived experiences, then the health benefits of treatment completion may not extend equitably across racial groups. The current study is the first to investigate racial differences in the impact of treatment completion on subsequent levels of optimism among justice-involved adolescents.
Methods: Ordinal regression was employed to analyze a sample of 2,000 opioid users in the Florida Department of Juvenile Justice (FLDJJ). This sample represents individuals who were processed by FLDJJ between 2005 and 2015, completed the full FLDJJ intake assessment, and self-reported opioid misuse in past 30-days. Individuals are asked about their substance use and level of optimism during enrollment interviews.
Results: Treatment completion was associated with higher levels of optimism in the total sample, but the benefits of treatment completion on optimism were significantly diminished among Black adolescents relative to White adolescents and Latinx adolescents. Compared to those who did not complete treatment programs, Treatment completion was associated with a 26% increased likelihood of normal or high optimism among White individuals, a 6% increased likelihood of normal or high optimism among Black individuals, and 31% increased likelihood of normal or high optimism among Latinx individuals.
Conclusions: Equal access to treatment may not sufficiently resolve racial differences if these interventions do not provide equitable levels of recovery capital. Researchers should investigate how systemic racism may obstruct treatment outcomes.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

S18. Reductions in Blood Alcohol Concentration During the First 90 Days of a Telehealth Program for Alcohol Use Disorder

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Drug Category Alcohol
Topic Treatment
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Few people with alcohol use disorder (AUD) receive evidence-based treatment. Telemedicine may help people engage in AUD treatment by offering support that is geographically available and private. The Ria treatment platform was launched in 2017 and uses telemedicine to provide AUD treatment that is tailored to the goals of patients, including goals of abstinence or controlled drinking. Ria offers management of AUD medications from a health-professional (expert physician or psychiatric nurse practitioner), regular visits with recovery coaches, didactic learning materials, and a breathalyzer to calculate blood alcohol concentration (BAC) up to twice daily. In this retrospective longitudinal study, we characterize clinical services and changes in BAC observed over the first 90 days of participation in RTP.
Methods (Optional): Patients (n=1840) who provided BAC data at least 90 days into the program and completed intake evaluations in which they report their demographics and treatment goals were evaluated. We used frequency statistics to characterize clinical services and longitudinal latent growth curve models to characterize trajectories of mean BAC over time.
Results (Optional): Out of 3730 patients who provided BAC data, 1840 (49.3%) provided BAC data at least 90 days into treatment and were included in the analytic sample described below. Most patients were female (52.1%) and had a goal of controlled drinking (65.5%). The median age was 50. During the first 90 days, 92.7% of patients met with a health professional, 96.0% met with a recovery coach, 91.5% were prescribed at least one medication, and there was a mean of 92.8 (SD=49.0) BAC readings provided per patient. Trajectory-estimated mean BAC decreased significantly between day 1 (mean BAC = 0.065) and

day 14 (mean BAC = 0.032), then continued to significantly decrease through the 90th day (mean BAC = 0.021), with similar changes observed for patients with abstinence versus controlled drinking goals.
Conclusions: Patients who participated in a telehealth program offering medical and psychosocial AUD services for at least 90 days achieved substantial reductions in drinking based on an objective BAC measure. Delivering AUD services through telehealth may help patients with AUD engage in treatment and reduce their drinking.

S19. A Casual Model of Risk Factors Underlying Onset of Alcohol Use in Childhood

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Drug Category Alcohol
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Early alcohol sipping occurs in up to 50% of children before the age of 10 and is predictive of problematic alcohol use in adolescence and adulthood. Here, we use a data-driven approach to derive a casual graph of early sipping behavior that encompasses family-environment, health, and psychological risk factors.
Methods: We used a data-driven machine-learning approach to model causal relationships [Causal Discovery Analysis (CDA)] within a sample of children collected from 21 sites across the United States [Adolescent Brain Cognitive Development (ABCD) Study]. After excluding participants who reported accidental, furtive, and religious sipping and those with incomplete data (N = 8,807; 48% female, aged 9-10), 14% (N = 1,203; 41% female) reported sipping alcohol by age ten. Based on our previous machine-learning analysis ranking risk factors associated with early alcohol sipping, we used the top-ranked factors (6 family-environment, 6 health, 7 psychological) to derive a single causal graph encompassing a broad array of mechanisms contributing to early alcohol sipping.
Results: We found that two clusters of underlying factors drive sipping by age 10. One cluster encompassed family-related factors, including easy access to alcohol, high parental education, high child weekend screen time, and longer sleep times. The second cluster encompassed child-centered health factors, including passive suicidal ideation and low-level symptoms of prodromal psychosis. Notably, individual-level psychological factors included in the model that are classically associated with maladaptive behavior (e.g., sensation-seeking), did not causally influence early alcohol sipping.
Conclusions: Our findings suggest that both family- and child health-related factors causally influence early alcohol sipping. Notably, we found that mental health factors, even at the young age of 10, caused early alcohol sipping. This finding suggests that more research pertaining to early prevention, detection, and treatment of mental health problems in childhood may serve to protect against early sipping and thus future problematic alcohol-related behavior.
Financial Support: AMM is funded by the National Institute of Neurological Disorders and Stroke (T32NS105604-04; PI: Redish).

S20. A Rapid Procedure to Assess Shifts in Discriminative Control Over Drinking During Recovery-Like Behavior

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Drug Category Alcohol
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Previously, we developed an operant procedure using rats to assess shifts in discriminative control over alcohol use. A drinking phase (ETH, a stimulus signals that ethanol alone is available), is followed by varying numbers of recovery-like sessions (RCV, a distinct stimulus signals that both food and alcohol are available). In subsequent test sessions, rats were exposed to the ETH stimulus under extinction, and responses were recorded. Food responses during test sessions increased as a function of the number of RCV sessions completed. However, this procedure required repeated training and testing per time point. Thus, we

developed a more efficient procedure, allowing for continuous assessment of stimulus control over drinking across varying recovery time points. We extended the model by evaluating the impact of an extended period of drinking (ETH) and sex effects.
Methods: Male and female rats (n=55) responded under ETH conditions for either 10 or 20 consecutive sessions, then moved into the recovery-like phase where they responded under RCV conditions for 16 consecutive sessions. Prior to RCV sessions 0, 1, 2, 4, 8, and 16, rats were exposed to the ETH stimulus under extinction conditions and responses on food and ethanol levers were recorded. The total number of food responses during test sessions prior 5 responses for ethanol was the primary measure. Each measure was analyzed using repeated measures ANOVA with day of recovery and drinking status as factors.
Results: Consistent with the earlier procedure, the number of food responses during ETH tests increased as a function of the number of RCV sessions completed. There was a significant effect of recovery day $F[5, 198]=3.2$, $p<0.01$.
Conclusions: Consistent with the earlier procedure and clinical evidence, stimulus control over drinking decreases following longer periods of recovery. Under conditions tested, longer prior drinking history did not affect this relationship and sex differences were not apparent.
Financial Support: Funded by NIAAA Grant AA025664

S21. Open Board

S22. Perspectives of Health Consumers With HIV on Integration of Pharmacological Mental Health and Substance Use Treatment in HIV Care

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Drug Category Alcohol
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: Rates of mental health disorders and alcohol use disorder among persons living with HIV are disproportionately high. Many people living with HIV who have untreated encounter issues with retention in HIV care. Therefore, addressing and improving the integration of pharmacotherapy for mental health and alcohol use disorder in HIV care is a key component to increasing retention rates and ending the epidemic.
Methods: Virtual interviews (N=10) were conducted with healthcare consumers with HIV and comorbid mental health and substance use challenges (70% African American; 30% White) in the Atlanta metro area. Interviews assessed barriers and facilitators to assessing mental health and substance use disorder treatment and the appropriateness of HIV care providers treating mental health and substance use disorders. Rapid qualitative analysis was conducted to identify common themes for the interview transcripts, including the development of summary templates based on the interview guides, the review and discussion of templates to ensure intercoder reliability, and the completion of the templates for all transcripts by two coders.
Results: All participants indicated a desire for mental health and substance use treatment services. Primary barriers to treatment were awareness of services, stigma, and provider-related challenges to accessing services. Specifically, participants noted the lack of knowledge of available treatments and where to access them; HIV-, substance use-, and mental health-related stigma; and mistrust of providers are major barriers to treatment. Some clients reported some hesitancy about HIV care providers offering pharmacological treatment for mental health, preferring that providers "stay in their lane".
Conclusions: Findings indicate a desire for integration of substance use, mental health, and HIV services for people living with HIV. Addressing client concerns and barriers to pharmacotherapy and substance use services in HIV care can inform the development of new tools to integrate care, which is a critical strategy to improve retention in HIV care.
Financial Support: National Institute of Mental Health and National Institute on Drug Abuse 5R34MH124628

S23. US Treatment Admissions for Alcohol Use Disorder by Gender and Reproduction 2015-2019

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Drug Category Alcohol
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: To describe characteristics and patterns of alcohol use disorder (AUD) treatment admissions in the US by gender and reproduction.
Methods: The Treatment Episode Data Set Admissions (TEDS-A 2015-2019), restricted to reproductive aged (18-44) admissions, was used to describe patterns of AUD admissions between men, non-pregnant women, and pregnant people. Given the size of the data, standard frequentist statistics would inevitably yield "significant" results. Hence, results are reported as proportions.
Results: Of the 6,517,537 reproductive aged admissions, 1,665,074 were for AUD (1,144,887 men, 509,035 women, 11,152 pregnant). Overall, admissions for AUD were more common among men (29%) than non-pregnant women (23%) and least common in pregnancy (10%). There were minimal differences among AUD admissions by race, ethnicity, and marital status. Women and pregnant people had higher educational attainment than men. Pregnant people were younger. Co-use of methamphetamine was highest in pregnant admissions (13%) compared to men (6%) or non-pregnant women (8%). There were minimal differences between groups in other substance co-use: opioid use was rare (4%) and cannabis common (28%). The most common referral source was the criminal legal system for both men and pregnant people (37%, 35%), whereas individual/self-referral was most common for non-pregnant women (38%). There were no differences in prior treatment admissions (36% were initial and 10% had 5+ prior episodes). Most pregnant admissions reported no past month alcohol (52%) in contrast to men (27%) and non-pregnant women (26%) and only 17% reported daily drinking compared to 33% men and 32% non-pregnant women. Compared to men and non-pregnant women, pregnant admissions were less likely to detoxification (8% vs. 25% and 22%) and more likely to long-term (30+ days) residential programs (11% vs. 6%).
Conclusions: Drinking patterns prior to AUD treatment admission and treatment episodes differ more by reproduction than gender. Research on gender disparities should separate out reproduction when possible.

S24. Evaluation of the Adverse Effects of Synthetic Cathinones in Mice: Dependence and Toxicity

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Drug Category Club/Designer Drugs
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The abuse of new psychoactive substances causes serious health problems, and such abuse is a major social problem worldwide. Synthetic cathinones are amphetamine-type substances, and even if one cathinone is regulated, others are continually developed one after another. In the present study, we attempted to establish an assessment system for the rapid evaluation of the psychic-dependence liabilities and cytotoxicities of synthetic cathinones.
Methods: As in vivo screenings, the present study investigated the behavioral properties of synthetic cathinones in mice. The pharmacological targets of cathinones are dopamine, serotonin, and noradrenaline reuptake transporters (DATs, SERTs, and NETs, respectively). As in vitro screenings, the potency of DAT inhibitory effects was examined in DAT expression cells (HEK-DAT cells). The cytotoxicological effects of cathinones were characterized in mouse limbic neurons of primary culture in vitro.
Results: Abused cathinones (eight types) induced hyperlocomotion in mice. Similarly, in a place-conditioning study, cathinones produced a significant conditioned-place preference (CPP). In HEK-DAT cells, cathinones showed DAT inhibitory effects. A positive correlation was found between cathinone-induced hyperlocomotion or CPP and the potency of DAT inhibitory effects. Furthermore, our data on limbic primary culture indicated that cathinones have some level of neurotoxicity. These behavioral and neurochemical data suggest that cathinones have strong adverse effects and psychic-dependence liabilities.
Conclusions: The predominant action of all cathinones on DATs is probably associated with a risk of abuse/addiction. The potency of DAT inhibitory effects of cathinones could indicate the risk of abuse. With our drug-screening system, we could rapidly evaluate and quantify the psychic-dependence liabilities and

cytotoxicities of synthetic cathinones. The scientific data obtained from this screening system could contribute to legislation for the comprehensive designation of new psychoactive substances.
Financial Support: This research was supported by a Research Grant for Regulatory Science of Pharmaceuticals and Medical Devices, Health and Labour Sciences Research Grants from the Ministry of Health, Labour and Welfare of Japan (to M.F.).

S25. Contraceptive Literacy and Utilization Among Illegal Drugs-Involved Women in Community

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Drug Category Club/Designer Drugs
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Although an array of negative consequences of in-uterus drug exposure have been well documented, women's reproductive healthcare is often unaddressed in addiction treatments and services. The present study is aimed to investigate contraceptive literacy and utilization among the community-dwelling illegal drugs-involved women in northern Taiwan and to explore potential explanatory factors.
Methods: Building upon an on-going survey on the illegal drugs-involved adult women of reproductive age (i.e., 20-45 years old), the data were collected in the government-operated drug prevention centers and non-governmental organizations operated addiction recovery services in the community. Information concerning sociodemographic status, contraceptive utilization and literacy, adverse childhood experiences, gender role attitudes, and intimate violence experiences were assessed by computer-assisted self-interviewing standardized instrument.
Results: Among 50 respondents, 42% are under the age of 30 years and one quarter has ever been imprisoned for illegal drug use. Ketamine (72%), methamphetamine (14%), and heroin (8%) are the most commonly involved drugs, and 26% had the first use before the age of 18. The majority have high contraceptive literacy, with 96% reporting the easiness to make decisions to use contraceptives. Nevertheless, only one-fourth used any of contraceptives every time when having sexual intercourse in recent six months. Having higher adverse childhood experiences and gender role attitudes was positively linked with the number of pregnancies and contraceptive non-utilization.
Conclusions: A potential gap may exist in contraceptive literacy and utilization among illegal drugs-involved women in community. To facilitate addiction recovery, comprehensive treatment services should integrate reproductive healthcare. Interventions aimed at reducing unplanned pregnancy or negative pregnancy outcomes in the drugs-involved women may consider childhood experiences (e.g., adversity).
Financial Support: This study is supported by grants from the Ministry of Science and Technology (grants numbers 109-2629-B-010-001-MY3).

S26. Methylone Pre-Exposure Differentially Impacts the Aversive Effects of MDMA, MDPV and Fluoxetine in Male and Female Sprague-Dawley Rats

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Drug Category Club/Designer Drugs
Topic Drug Interactions
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The abuse potential of a drug is thought to be a balance of its rewarding/aversive effects, and several subject (e.g., sex) and experiential (e.g., drug interactions) factors impact this affective balance. In this context, the synthetic cathinones have recently examined to characterize these affective properties. The present study assessed the effects of a history with methylone, a first-generation synthetic cathinone that serves as a substrate releaser for DA and 5-HT, on taste avoidance induced by the synthetic cathinone MDPV (highly selective DA reuptake inhibitor), MDMA (5-HT substrate releaser) and the antidepressant

fluoxetine (selective 5-HT reuptake inhibitor). Drug history with specific drugs has been shown to reduce the aversive effects of a number of compounds, generally dependent on the similarity of their mechanisms of action.
Methods: Male and female Sprague-Dawley rats (n = 127) were exposed to vehicle or methylone (10 mg/kg) every 4th day for a total of five injections prior to taste avoidance conditioning in which a novel saccharin solution (1 g/l) was paired (five times) with MDMA (1.0 mg/kg), MDPV (1.8 mg/kg) or fluoxetine (10 mg/kg).
Results: Under these conditions, methylone pre-exposure attenuated the aversive effects of MDPV (males and females) and MDMA (only in males) [$p < 0.05$] while having no impact on the aversive effects of fluoxetine for either sex ($p > 0.05$).
Conclusions: Together, these results suggest that the effects of drug preexposure are drug and sex dependent. That the strongest attenuation occurred with MDPV (with only moderate effects with MDMA and no effect with fluoxetine) suggests that the aversive effects of methylone may be mediated by DA.
Financial Support: Supported by grants from the Center for Neuroscience and Behavior and the College of Arts and Sciences at American University (HM) and the Mellon Foundation (ALR).

S27. Trends in Drug Use Among Nightclub/Festival Attendees as a Potential Bellwether for Drug-Related Outcomes in the General Population

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Drug Category Club/Designer Drugs
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Nightclub/festival attendees are known to have high levels of drug use. This study aimed to determine whether use among this population can serve as a bellwether or indicator for use and use-related outcomes in the general population in New York (NY) and in UK countries.
Methods: Trends in past-year cocaine and methamphetamine use were estimated from nightclub/festival attendees in New York City and among NY residents, and trends were estimated for related death rates in NY (2014/15-2019). Using national data from England and Wales (2010-2019), trends in past-year cocaine and ecstasy use (among the full population and among those reporting nightclub attendance), seizures, and related deaths were also estimated.
Results: In NY, cocaine use remained stable in the general population, but use among nightclub/festival attendees doubled. There was also a 528.6% increase in cocaine-related deaths (involving opioids). Methamphetamine use among nightclub/festival attendees more than doubled while use among the general population remained stable, and rates of related deaths increased overall—whether or not opioid use was involved. In UK countries, increases in cocaine use were larger for infrequent/frequent nightclub attendees compared to the general population, with a 360.7% increase in related deaths. Ecstasy use remained stable but increased among infrequent/frequent nightclub attendees. Ecstasy-related deaths also increased 805%.
Conclusions: Patterns of drug use among nightclub/festival attendees, more so than patterns in the general population, appear to be similar to patterns of drug-related deaths. Use among this subpopulation could possibly serve as a bellwether for use-related outcomes in the general population.
Financial Support: National Institute on Drug Abuse

S28. Methodological Considerations for the Human Abuse Potential Evaluation of Emerging Drug Therapies With Psychedelic Properties

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Drug Category Psychedelics
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Theoretical/Commentary

Aim: Methodological exploration of the abuse potential assessment of psychedelic drugs.
Methods (Optional): Interest in the use of psychedelics for the treatment of various psychiatric conditions has re-emerged in recent years. As drug candidates proceed through the drug development process, assessment of abuse potential will be a critical factor. Psychedelics' unique characteristics will likely require modifications to the standard assessments incorporated in the human abuse potential (HAP) study, one of the key trials for determining if a drug exhibits pharmacological traits that make it appealing for abuse. Typically, the primary endpoint of the HAP study is the visual analog scale (VAS) for Drug Liking. Most drugs with known abuse potential (eg, opioids, stimulants) have positive endorsements on Drug Liking and other pleasurable effect measures (eg, Good Drug Effect, High). Psychedelics are associated with altered, affectively intense sensory distortions and changes of thought processes, which can be perceived as highly enjoyable or extremely unsettling ("bad trip"). These effects are often unpredictable, including in the same person on different occasions, and thus 'Drug Liking' may have highly variable outcomes and be a less reliable measure for this drug class. A holistic evaluation of various measures, including those that evaluate perception altering effects, may be more suitable for predicting the abuse potential of psychedelic drugs.
Conclusions: Assessments currently utilized in HAP studies including the Bowdle VAS, Addiction Research Center Inventory (LSD-items), along with 'standard' VAS (eg, Drug Liking, Take Drug Again), and other scales eg Clinician-Administered Dissociative States Scale and Mystical Experience Questionnaire, may be considered. Various other methodological adaptations to HAP studies are also reviewed, including appropriate inclusion/exclusion criteria, selection of positive controls, selection of appropriate doses, the qualification phase, timing of pre- and post-dose measures, maintaining blinding, and ensuring subject safety.
Financial Support: Altasciences

S29. Use of Plant-Based Hallucinogens and Dissociative Agents: U.S. Time Trends, 2002-2019

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Drug Category Psychedelics
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Information on time trends in use of specific plant-based hallucinogens is lacking. The current study assessed overall and age-specific time trends in the prevalence of lifetime and 12-month use of specific plant-based hallucinogens and dissociative agents in the US using nationally representative data.
Methods: Participants were respondents aged ≥12 years (N=1,006,051) from the National Survey on Drug Use and Health (NSDUH), 2002-2019. Predictors were continuous years. Outcome variables included illicit (non-medical) use of peyote, mescaline, psilocybin, ketamine, salvia, and tryptamine. Sociodemographic variables (gender; age; race/ethnicity; educational level; family income) were modeled as covariates. Trends were estimated overall and by age (12-17, 18-25, 26+). Prevalence differences [PDs] were obtained for each category, and significance was determined through a 95% confidence interval [CI] not including 0.0.
Results: Increases in lifetime use were observed for psilocybin (2002-2019 PD=+1.61, tryptamine (2006-2014 PD=+0.55; 2015-2019 PD=+0.44), and ketamine (2006-2014 PD=+0.27; 2015-2019 PD=+0.21). Mescaline use decreased (PD=-0.89). While overall lifetime salvia use increased between 2006-2014 (PD=+1.81), prevalence did not change between 2015-2019. Twelve-month use of tryptamine and ketamine increased between 2006-2014 (PD=+0.14; +0.03, respectively). Twelve-month ketamine use also increased from 2015-2019 (PD=+0.03), while tryptamine use did not. By age, participants age 12-17 and 18-25 showed decreases in use of most types of hallucinogens, while those age 26 and older generally showed increases.
Conclusions: While use of plant-based hallucinogens and dissociative agents remains rare in the general population, lifetime use of ketamine, tryptamine, and psilocybin is increasing in adults. Notably, substances with consistent increases in illicit use over time (ketamine, psilocybin) occur simultaneously with research regarding the extent of their therapeutic benefit. Considering these increases alongside interest in the therapeutic utility of certain hallucinogens, clinicians and policymakers should remain mindful of the already rising rates of use in the general population to enable informed decision making.
Financial Support: T32DA031099 (Hasin), New York State Psychiatric Institute

S31. Exploring the Heteromeric Interface of the Serotonin 5-HT2A:5-HT2C Receptor Complex In Vitro

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Drug Category Psychedelics
Topic Molecular Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Enrichment of serotonin 5-HT2A receptor (5-HT2AR) function may be useful in combating substance use disorders (SUDs). The 5-HT2AR heterodimerizes with the 5-HT2CR and, when the two receptors are in complex, 5-HT2AR signaling is silenced. Thus, disruption of this 5-HT2AR:5-HT2CR complex provides an opportunity to selectively enhance 5-HT2AR function. In the present study, we are testing the hypothesis that impeding the 5-HT2AR:5-HT2CR interface will uncover enhanced 5-HT2AR signaling output.
Methods: A split luciferase complementation assay (LCA) was employed to assess the direct coupling of h5-HT2AR and h5-HT2CR in live HEK293 cells. The cDNA for the each receptor was fused with complementary C-terminal (CLuc) and N-terminal (NLuc) inactive fragments of luciferase, respectively, and transfected. Association of the receptor constructs within ~50 nm reconstitutes luciferase activity and light is released in the presence of D-luciferin. The expression of the activity-regulated immediate early gene early growth response 1 (EGR1) was used to trace cellular responsivity to 5-HT in cells. A truncated version of the 5-HT2CR transmembrane helix IV (TM4) domain conjugated to a polyethylene glycol chain was synthesized as a tool to disrupt the 5-HT2AR:5-HT2CR complex.
Results: Robust complementation (i.e., increased luminescence) between the 5-HT2AR and 5-HT2CR was observed in vehicle-treated cells. Robust expression of EGR1 was observed upon 5-HT treatment within cells solely expressing 5-HT2AR, but not the 5-HT2CR; 5-HT-evoked EGR1 expression was blunted in 5-HT2AR:5-HT2CR cells which was reversed by treatment with the TM4 peptide in a concentration-dependent manner.
Conclusions: These data support the probability that the assembly of the 5-HT2AR:5-HT2CR complex in vitro is dependent on the TM4 interaction interface. Our ongoing studies will elucidate mechanisms by which receptor heteromerization modulates the pharmacological properties of the 5-HT2AR and will validate the interaction interfaces between the 5-HT2AR and 5-HT2CR as druggable targets for SUDs.
Financial Support: Supported by DA033935, P50DA033935 and the UTMB Center for Addiction Research

S32. Open-Access Clinical Care and Intervention in the Setting of Overprescribing of Benzodiazepines in a Community Sample

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Drug Category Sedative/Hypnotics
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Amid the current COVID-19 pandemic, addiction treatment centers have been concerned with the consequences of COVID for patients with SUD; the worsening opioid epidemic and the toxic mix of benzodiazepine prescriptions midst these converging health care catastrophes. During the pandemic, more than 110 patients in the APT Foundation's clinical programs were receiving psychiatric care from an outside provider in the New Haven community whose practice was closed because of medical malpractice related to over-prescribing of controlled substances, principally benzodiazepines. The aims of this study were to examine the effectiveness of an open-access approach to patients caught in the crosshairs of prescriber induced benzodiazepine dependence and systems of care at maximal capacity.
Methods: 110 existing OTP patients from the precipitously closed psychiatric practice sought psychiatric care at the APT Foundation. These individuals participated in mental health evaluations and completed the BASIS-24. All patients were told that psychiatric providers would not necessarily continue benzodiazepines

prescriptions, that we would consider underlying psychopathology and medical co-morbidities and that patients would be respected interlocutors in their care.
Results: This sample includes 83 participant. Average age was 47.2 years. 54 were male and 29 were female. Racial makeup: 92% white, 5% multiracial and 1% black. 47% of participants had completed HS or a GED; 7% were in a marriage or partnership; 72% were unemployed. 54% of the individuals in the study felt depressed at least half of the time; nearly 20% endorsed mood swings throughout the day.
Conclusions: 90% of patients who were a part of the closed prescriber's practice and who sought care at APT continue in our care since their psychiatric evaluation. These individuals are on reduced doses of benzodiazepine or tapered off completely. Greater than 60% of participants are on medications appropriate to underlying psychiatric diagnoses. Medication changes were negotiated with patient readiness in mind.
Financial Support: APT Foundation, Inc.

S33. Human Abuse Potential Study Results in the Context of Abuse Detected Postmarketing

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Drug Category Sedative/Hypnotics
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: A positive signal in a human abuse potential (HAP) study may not always translate to high levels of actual drug abuse. This may be most evident in drugs determined to have a low potential for abuse in HAP studies.
This study was conducted to determine whether additional data collection and analyses on subjective measures may offer a better understanding of abuse detected post-marketing.
Methods: We analyzed data from several HAP studies submitted to the FDA as a basis for placement in schedules IV or V, in which visual analog scales (VAS) were used to measure subjective effects such as drug liking, feeling good, feeling bad, and other drug effects, for the test drugs, positive controls and placebo. To evaluate cases of abuse detected postmarketing, drug utilization and epidemiological data of abuse, and related adverse outcomes were collected from 2010-2020.
Results: For all HAP studies analyzed, the mean values for Emax scores to positive subjective effects such as Drug Liking, Take Drug Again, Overall Drug Liking, were greater than placebo and similar to those produced by the positive control. Findings of epidemiological data yielded few cases of abuse involving the drugs of interest.
Conclusions: There may be several reasons why the abuse detected postmarketing may not be consistent with positive signals from HAP studies and further research is necessary.

S34. Ketamine Non-Medical Use Versus Medical Use in the United States' General Population

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Drug Category Sedative/Hypnotics
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Ketamine is used medically to treat pain and depression but also abused non-medically due to its dissociative and hallucinogenic properties. This study aims to describe medical versus nonmedical use of ketamine in the U.S. through evaluating its wide range of users.
Methods: The Survey of Non-Medical Use of Prescription Drugs Program is a repeated cross-sectional online survey of adults in the U.S. which provides estimates of the non-medical use of prescription drug classes and non-pharmaceutical drugs. A total of 29,845 respondents were collected in 3rd quarter 2021, and calibration weighting was utilized to represent the general population of adults. Non-medical use (NMU) of ketamine was defined as use of pharmaceutical forms in a way not directed by a healthcare professional or

any use of a non-pharmaceutical form. Prevalence of ketamine use as intended vs NMU, demographics, and other drug-use was assessed.
Results: The estimated prevalence of any lifetime use of ketamine was 3.4% (95% CI: 3.2 – 3.7), representing 8,851,120 U.S. adults. A total of 2% (1.9 – 2.2) of the U.S. population has used ketamine non-medically in their lifetime; a total of 1.4% (1.3-1.6) only ever used medically as intended. Mean DAST-10 scores for adults who only used medically as intended was 1.4 (95% CI: 1.2 – 1.6) and 3.0 (2.7 – 3.2) for non-medical users. Adults who non-medically used were primarily white (81.6%), male (66.7%), and had used cigarettes (60.0%), cannabis (78.4%), or alcohol (61.6%) in their lifetime. Among adults who non-medically used, notable percentages were healthcare professionals (12.2%), veterans (11.2%), unemployed (50.0%), or students (15.4%).
Conclusions: NMU of pharmaceutical or use of nonpharmaceutical ketamine in the U.S. accounts for most of the lifetime use of the drug. Adults who NMU have more serious substance use profiles than those who use as intended, exposing them to other risks.
Financial Support: The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado. The RADARS System is supported by subscriptions from pharmaceutical manufacturers, government and non-government agencies for surveillance, research and reporting services. Subscribers did not participate in data collection or analysis of this abstract.

S35. Perspectives of People Who Use Illicit Stimulants on Prospective Pharmaceutical Stimulant Substitution Treatments: A Qualitative Study

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Drug Category Stimulants
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To identify perceptions of prospective pharmaceutical stimulant substitution treatments (SST; e.g., Dexedrine, methylphenidate) for people who use illicit stimulants and their role in addressing treatment gaps for illicit stimulant use.
Methods: In-depth qualitative interviews were conducted with 86 PWUS in Vancouver, Canada. Thematic analysis of interviews focused on perceptions and experiences of available treatment programs for stimulant use, treatment needs, and perceptions of prospective pharmaceutical substitution treatment for stimulant use disorder.
Results: Participants challenged perceptions of PWUS as treatment resistant, rather, identifying how current treatment approaches do not meet the unique needs of PWUS. Participants described how these current approaches are behavioural, contrasting this with the range of medical treatments available for opioid use disorder. If given the opportunity to access SST, participants emphasized the health and social benefits they could anticipate from a medical model of stimulant treatment, including avoiding the toxic supply of illicit stimulants, reduced engagement in criminalized activities, as well as economic benefits. Perceptions of prospective SST were informed by knowledge of existing opioid substitution and agonist therapies, leading some participants to be unsupportive of SST, citing the loss of agency requisite of participation in opioid-related treatments, and highly regulated operational contexts that do not align with the lived realities of stimulant use (e.g., sporadic usage, binge use).
Conclusions: Given emerging clinical evidence suggesting the effectiveness of pharmaceutical alternatives for illicit stimulants, our findings demonstrate the need for SST pilot programs in real-world settings, and underscore the health and social advantages SST may offer; although reproducing drawing on existing opioid treatment models to implement an SST pilot may limit its success. Thus, our findings highlight the need to centre the lived realities of PWUS in any novel treatments for stimulant use.
Financial Support: Canadian Institutes of Health Research

S36. Abuse Potential of Zuranolone in Nondependent, Recreational Users of Central Nervous System Depressants: A Randomized, Double-Blind, Active- and Placebo-Controlled, Crossover Study

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Drug Category Other, Neuroactive steroid and positive allosteric modulator of GABAA
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: Zuranolone, an oral neuroactive steroid and positive allosteric modulator of GABAA receptors, is under investigation between 30 and 50 mg as a once-daily, 2-week therapy for major depressive disorder and postpartum depression in adults. We hypothesized zuranolone 30 and 60 mg would have lower abuse potential vs alprazolam.
Methods: This 2-part, double-blind, active- and placebo-controlled study enrolled healthy nondependent, recreational users of CNS depressants. The dose-selection phase assessed zuranolone (60, 80, and 90 mg) vs placebo in a parallel-group design. In the main study, participants received zuranolone (30, 60, and 90 mg), alprazolam (1.5 and 3 mg), and placebo in a randomized, 6-way crossover manner. The primary endpoint was peak effect score (Emax) for Drug Liking, evaluated using a linear mixed-effects model. Key secondary endpoints included Overall Drug Liking and Take Drug Again Emax and adverse events (AEs).
Results: During the main study, zuranolone 30 and 60 mg demonstrated significantly less Drug Liking Emax vs alprazolam 1.5 and 3 mg ($p<0.05$ for all); there was no significant difference for zuranolone 90 mg vs alprazolam. For Overall Drug Liking, zuranolone 30 and 60 mg demonstrated significantly lower Emax vs both alprazolam doses ($p\leq0.005$). For Take Drug Again, zuranolone 30 mg demonstrated significantly lower Emax vs both alprazolam doses ($p<0.001$). Zuranolone 60 mg demonstrated significantly lower Emax vs alprazolam 3 mg ($p=0.003$); and 90 mg did not differ significantly from alprazolam. AEs were mostly mild. In the main study, common AEs (≥5% occurrence) for zuranolone 30 and 60 mg included somnolence, fatigue, and euphoric mood. No participants discontinued due to AEs.
Conclusions: Zuranolone 30 and 60 mg demonstrated lower abuse potential vs alprazolam 1.5 and 3 mg; 90 mg was comparable to alprazolam. Zuranolone was generally well tolerated, with a safety profile consistent with phase 2 and 3 studies.
Financial Support: Study supported by Sage Therapeutics, Inc.

S37. The Association Between Childhood Trauma, Intimate Partner Violence and Perceived Parental Competence Among Women Abusing Amphetamine Type Stimulant

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Drug Category Stimulants
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Intimate partner violence is a complex issue with multiple factors leading to it. This study looks into the correlation between childhood trauma, intimate partner violence (IPV) and perceived parenting competence of women abusing methamphetamine in a rehabilitation centre.
Methods: This cross-sectional study recruited 106 participants, 88 of which were mothers. The Childhood Trauma Questionnaire Short Form, Parenting Sense of Competence Scale, Mini International Neuropsychiatric Interview version 6, and the Women's Health and Life Experiences Questionnaire was used for data collection.
Results: This study revealed that childhood emotional abuse and physical neglect were the most reported types of childhood trauma at 66% and 39.6%, respectively. As for interpersonal violence, 70.5% of these women experienced physical trauma and 30.5% experienced sexual trauma from their partners. A history of childhood emotional abuse significantly raises the probability of these women experiencing sexual violence from their partners by 20.9%. This study also reveals that women with childhood trauma, namely emotional neglect, emotional abuse and physical abuse, tend to perceive themselves as less competent parents. Similarly, childhood emotional and physical abuse was negatively correlated with parenting satisfaction.
Conclusions: The current study highlighted a worrying fact that a majority of substance abusing women had experienced childhood trauma. These affected women are then at further risk of interpersonal violence which may worsen their substance use disorder. An emphasis on children's wellbeing and safety against

domestic violence should be given to help reduce the likelihood of similar situations happening to women elsewhere.
Financial Support: This study was partially funded by the Ministry of HIgher Education (MoHE) Malaysia (grant number LRGS/1/2019/UKM/02/2/3) and Universiti Kebangsaan Malaysia Medical Centre.

S38. The Risk Factors of One-Year Relapse Among Methamphetamine Users Referred From Criminal Justice System for Mandatory Treatment

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Drug Category Stimulants
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Methamphetamine (MA) use disorder is associated with a high likelihood of relapse. However, little is known regarding the clinical predictors of relapse that is critical to develop a more tailored prevention program.
Methods: We recruited participants who received court-mandated treatment for 1st time drug offenders of MA use in Taipei City Hospital from January 2016 to and August 2018. We used t-test to compare socio-demographic characteristics, psychological symptoms, substance use comorbidities and life satisfaction between relapse and non-relapse group in one year follow-up. In addition, we used multivariate cox regression model to identify risk factors associated with MS relapse use.
Results: One-year relapse rates of MA use was 38%, with the mean number of days of abstinence 66.8 (SD: 84.5). Compared to non-relapse group, the relapse group had a lower education level, younger age of drug use onset, longer length of drug use, use, higher craving severity, higher levels of depressive and anxiety symptoms, and lower life satisfaction. Baseline urine test positive for MA was associated with a 3.85-fold increase in the risk of relapse compared with those who showed negative drug test at baseline. In the multivariate cox regression model, we found craving severity and baseline positive urine results were associated with shorter time to relapse, while socio-demographic characteristics, psychological symptoms, and substance use pattern were not.
Conclusions: Craving and baseline positive urine drug test were associated with higher risk of MA relapse in court-mandated treatment program. Future intervention should incorporate these factors to develop a more tailored treatment program.
Financial Support: Taiwan Ministry of Science and Technology: 109-2628-B-532

S39. The Safety and Feasibility of Lisdexamfetamine for the Treatment of Acute Methamphetamine Withdrawal: Preliminary Results of an Open Label Pilot Study

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: There are no evidence-based therapies or medications for the treatment of methamphetamine (MA) withdrawal. This study aimed to assess the safety and feasibility of a 5-day, tapering dose regimen of lisdexamfetamine dimesilate (LDX) for the treatment of acute MA withdrawal.
Methods: A single-arm, single-site, open-label pilot study. Participants were inpatients in a drug and alcohol withdrawal unit, and received a tapering dose of LDX over five days: 250mg LDX on Day 1, reducing by 50mg per day to 50mg on Day 5. All participants also received standard inpatient withdrawal care. Participants were followed-up on Days 14, 21 and 28. Primary endpoint was safety at Day 5 (measured by adverse events and vital signs), and feasibility (time to recruit to study and screen failure rates).

Results: Ten participants enrolled (9 male [90%], mean age 37 [SD 6] years). Eight (80%) participants were retained to the primary endpoint and received all study medication doses, two (20%) left inpatient admission following second and third doses (unrelated to the study). All participants reported at least one adverse event (n=6 [60%] nausea; n=3 [30%] difficulty sleeping; n=3 [30%] hot flushes; n=2 [20%] mood fluctuations; n=2 [20%] headache, n=2 [20%] itch]). One AE was graded as serious and un-related to study treatment (progression of pre-existing shigellosis). No treatment-related serious adverse event was recorded.
39 potential participants were pre-screened for the trial, ten progressed to formal screening. Seven participants were recruited within the first three months, and an additional three during local COVID-19 restrictions.
Conclusions: This is the first trial of LDX for the treatment of MA withdrawal. We implemented a tapering regimen commencing at doses significantly higher than used for other indications. In our sample LDX was feasible and safe, with an AE profile consistent with the product label.
Financial Support: This research is funded by the National Centre for Clinical Research on Emerging Drugs (NCCRED). NCCRED is funded by the Australian Government Department of Health.

S40. Trajectories of Prescription Stimulant Misuse and Substance Use Disorder Symptoms From Ages 18 to 50: US National Panel Data

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Drug Category Stimulants
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To examine 32-year prescription stimulant misuse (PSM) trajectories and associations between PSM trajectories and substance use disorder (SUD) symptoms in middle adulthood.
Methods: Data were from 11 cohorts of nationally representative US high school students (N=26,575) followed longitudinally via self-administered surveys from modal ages 18 (1976-1986) to 50 (2008-2018) in the Monitoring the Future study. First, latent profile analysis was used to create PSM trajectory profiles based on PSM frequency at baseline and each of the ten follow-ups. Second, logistic regression models including controls were fitted using the generalized estimating equations methodology to assess the associations between these PSM trajectories and DSM-based SUD symptoms at ages 35-50.
Results: An estimated 34.8% (95% CI=34.1%-35.5%) of individuals reported past-year PSM at least once during the study period. We identified six distinct PSM trajectories: (1) Age 18-Peak, (2) Age 19/20-Peak, (3) Age 25/26-Peak, (4) Age 40-Peak, (5) Age 45-Peak, and (6) Age 50-Peak. Each of the six PSM trajectories had significantly higher prevalence of two or more SUD symptoms from ages 35-50 (prevalence ranged from 53.6% to 88.4%) compared to population controls reporting no PSM (prevalence was 29.8%). Likewise, all six PSM trajectories had significantly increased odds of two or more SUD symptoms from ages 35-50 when compared to population controls, controlling for relevant covariates. The four later peak PSM trajectories had significantly higher prevalence of two or more SUD symptoms from ages 35-50 than the two earlier peak PSM trajectories, controlling for relevant covariates.
Conclusions: Prescription stimulant misuse at all ages is a signal for substance-related problems, with SUD symptoms during middle adulthood being more common among people with later peak PSM trajectories than PSM trajectories that peak in late adolescence. Increased screening and monitoring for PSM is warranted given the long-term risks associated with misuse of these controlled medications.
Financial Support: Supported by research awards 75F40121C00148 from the Food and Drug Administration and research awards R01DA001411, R01DA016575, R01DA031160, R01DA036541, R01DA042146, UH3DA050252, and R01DA043691 from the National Institute on Drug Abuse and the National Institutes of Health.

S41. What's Driving the Increases in Methamphetamine Overdose Deaths That Do Not Involve Opioids?

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Drug Category Stimulants

Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Methamphetamine overdose deaths that do not involve opioids continue to rise, but the factors driving these increases remain unclear. Historically, overdose deaths involving methamphetamine without opioids have been rare. This presentation explores the contribution of older methamphetamine users with age-related comorbidities on these increases.
Methods: We analyzed CDC-WONDER data from 2017-2019 to assess changes in the characteristics of people who died from methamphetamine overdoses that did not involve opioids. We compared the characteristics of people who died from methamphetamine-only overdoses to the characteristics of people entering treatment for methamphetamine use in the Treatment Episode Dataset-Admissions (TEDS-A) between 2017-2019 to assess differences in the characteristics of people involved in fatal methamphetamine-only overdoses and those entering treatment for methamphetamine who may be somewhat more representative of methamphetamine users in general.
Results: Methamphetamine-only overdose related death data from CDC-WONDER confirm that individuals with heart conditions have a pattern of death that differs significantly from all individuals, not accounting for age. Specifically, the latter exhibit a peak in deaths between the ages of 35-44, while the former (individuals with heart conditions) exhibit a peak at the ages of 55-64. Additionally, treatment admissions data from the same time period (2017-2019) reveals a peak in individuals aged 25-34 entering treatment for methamphetamine use (i.e. using methamphetamine). TEDS-A data also show some increase in older individuals seeking treatment for methamphetamine use across time.
Conclusions: These data suggest varying patterns of use and death across age groups, which should be examined further with existing administrative data to test for additional hypotheses. These hypotheses may include the exacerbation of underlying medical comorbidities by methamphetamine use, evolving composition of methamphetamine across time, among others. Understanding the trajectory of older individuals using methamphetamine can be of use when tailoring clinical interventions to this population.

S42. Is Age of Onset and Duration of Stimulant Medication Therapy for ADHD Associated With Stimulant Misuse During Adolescence? A Multi-Cohort National Study

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Drug Category Stimulants
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To assess whether age of onset and duration of stimulant therapy for attention-deficit/hyperactivity disorder (ADHD) are associated with cocaine, methamphetamine, and prescription stimulant misuse during adolescence.
Methods: Data were from sixteen annual surveys (2005-2020) of nationally representative samples of US 10th and 12th grade students (N=150,395) surveyed via self-administered questionnaires. The sample represents a population that was 51.0% female, 55.0% White, 11.6% African-American, 15.6% Hispanic, and 17.8% other race/ethnicity. Design-based logistic regression analyses tested the associations between age of onset and duration of stimulant medication therapy for ADHD and stimulant misuse, controlling for potential confounders.
Results: An estimated 8.2% of youth received stimulant medication therapy for ADHD during their lifetime. More than one in ten of all youth reported past-year prescription stimulant misuse (10.4%); cocaine (4.4%) and methamphetamine use (2.0%) were less prevalent. Youth who initiated early stimulant therapy for ADHD (≤age 9) for longer duration (≥6 years) had significantly lower odds of cocaine or prescription stimulant misuse in adolescence than those initiating later stimulant medication therapy for ADHD (≥10 years) for shorter duration (<1 year). There were no differences in the likelihood of cocaine and methamphetamine use between individuals who initiated early stimulant therapy for ADHD (≤age 9) and for longer duration (≥6 years) and population controls (non-ADHD and unmedicated ADHD youth).
Conclusions: Youth who initiate early stimulant therapy for ADHD (≤age 9) for longer duration (≥6 years) do not have an increased risk of cocaine and methamphetamine use versus population controls during

adolescence. Later onset (≥10 years) and shorter duration (<1 year) of stimulant therapy for ADHD are significantly associated with cocaine, methamphetamine, and prescription stimulant misuse versus population controls during adolescence. Clinicians are encouraged to screen youth for ADHD and when initiating stimulant therapy for ADHD in secondary school monitor for the potential for stimulant misuse.
Financial Support: Supported by a research award 75F40121C00148 from the Food and Drug Administration and research awards R01DA001411, R01DA016575, R01DA031160, R01DA036541, UH3DA050252, and R01DA043691 from the National Institute on Drug Abuse and the National Institutes of Health.

S43. Novel Pharmacotherapies for Young People With Methamphetamine Use Disorder: The MASKOT and CALM Studies

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Methamphetamine use commonly starts in adolescence or early adulthood. New treatment approaches for young people are required. The aim of these two studies is to assess candidate pharmacotherapies for safety and tolerability in young people (15-25 year olds) with methamphetamine use disorder who wish to reduce their use.
Methods: The MASKOT study (MethAmphetamine use in young people: Sub-anaesthetic ketamine open-label trial; ACTRN12621000528853) is an open-label trial of sub-cutaneous ketamine. Participants (N=20) will receive two doses one week apart (initial dose 0.75mg/kg), with follow-up at weeks 2, 3, 4, and 6. Primary endpoints are safety (assessed by change in past month use of ketamine, and liver function tests at week 2) and tolerability (number of participants withdrawing from the study due to adverse medication effects). The CALM study (Cannabidiol – A novel pharmacotherapy for Lowering Methamphetamine use) is an open-label trial of cannabidiol (800-1000mg/day). Participants (N=12) will complete 8 weeks of oral cannabidiol, with follow-up at weeks 4, 8, and 12. Primary endpoints are safety (liver function tests at weeks 4 and 8) and tolerability (number of participants withdrawing from the study due to adverse medication effects). We hypothesized that ketamine and cannabidiol will have an acceptable safety and tolerability profile.
Results: To date, one participant has completed the MASKOT study (n=1). In the first session, they reported severe dissociation 60min post ketamine administration. The dose was reduced to 0.6mg/kg in the second session, which was well tolerated. There were no changes in liver function at week 2, and no changes in past-month use of ketamine at any of the follow-ups assessments. The CALM study will commence recruitment in early 2022. Both studies will be completed end of 2022.
Conclusions: Recruitment is ongoing for both studies. They will provide feasibility and tolerability data on two candidate pharmacotherapies in young people with methamphetamine use disorder.
Financial Support: National Centre for Clinical Research on Emerging Drugs (NCCRED) Seed Funding Grants

S44. Prevalence of Stimulant Use Disorder and Co-Occurring Substance Use Disorders Among Medicaid Enrollees With Stimulant Use Disorder in 2017-2018

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Recent trends show overdoses involving stimulants are increasing, which are part of a growing polysubstance use landscape. Individuals with substance use disorders (SUDs) involving multiple drugs were more likely to have an adverse event than those with just stimulant use disorder (StUD). Medicaid

finances a substantial proportion of SUD treatment and accounts for a majority of SUD population. We examined the prevalence of StUD and the demographic characteristics associated with polysubstance use among a nationally representative sample of Medicaid enrollees.
Methods: We conducted a retrospective national study using the Transformed Medicaid Statistical Information System data. The database includes all 50 states and DC and is representative of Medicaid enrollees nationally. The sample consisted of all Medicaid-eligible who were enrolled in Medicaid from 2017 to 2018 and had a StUD diagnosis on at least one claim. Multivariable logistic regression was used to examine the demographic characteristics associated with polysubstance use among Medicaid-enrollees with StUD.
Results: Of the ten million Medicaid enrollees, there were 378,618 (3.7%) individuals with a StUD diagnosis. Among those with a StUD diagnosis, common comorbid SUDs included opioid (37.3%), nicotine (24.2%), alcohol (18.0%), and cannabis (14.1%). Characteristics associated with increased odds of reporting polysubstance use include males [adjusted odds ratio (aOR) = 1.13, 95% confidence interval (CI) = 1.02-1.24]; age 25-34 years compared to those age 35-44 years (aOR = 1.21, CI = 1.16-1.26); unmarried [aOR=1.18, CI=1.06-1.31]; and non-Hispanic whites compared to non-Hispanic blacks (aOR = 1.31, CI =1.15-1.50].
Conclusions: The majority of individuals who were enrolled in Medicaid from 2017 to 2018 and were diagnosed with StUD appeared to be have at least one comorbid SUD. Despite non-Hispanic whites having higher odds of having a comorbid SUD, non-Hispanic blacks are more likely to experience an adverse event. This implies that greater understanding of prevention approaches is needed.
Financial Support: Research was supported by the National Institute on Drug Abuse (P30DA040500).

S45. Open Board

S46. Risk and Preventive Factors Associated With Illicit Drug Use Among Male Methamphetamine Users on Probation in Japanese Criminal Justice System: A One-Year Prospective Cohort Study

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Drug Category Stimulants
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Methamphetamine use is an increasing problem due to severe psychiatric and physical health problems and impacts from the social and criminal justice system. This study aimed at examining risk and preventive factors associated with the resumption of illicit drug use among methamphetamine offenders on probation in the Japanese criminal justice system.
Methods: We used data of males on probation due to individual methamphetamine use or possession in a multicentered prospective cohort study, “Voice Bridges Project.” The participants were recruited at the probation office and referred to public mental health centers. Healthcare workers at public mental health centers conducted a telephone-based survey and collected data. We selected participants who completed the one-year follow-up survey. The dependent variable was at least one illicit drug use event between the baseline and one-year follow-up survey. Multivariable logistic regression was performed to assess the association between illicit drug use and potential predictors, such as sociodemographic variables, the severity of drug use, and use of welfare or treatment services. This study was approved by the Institutional Review Board of the National Center of Neurology and Psychiatry. This study was supported by Health Labour Sciences Research Grant.
Results: Among the participants (N=175), 14 (8.0%) used any illicit drug during the one-year follow-up. After adjusting for sociodemographic variables and the severity of drug use, the use of welfare services was positively associated with illicit drug use (OR: 9.42, 95% CI: 2.07-42.9, $p<0.01$). Trust relationship with others and unemployment at the baseline were negatively associated with illicit drug use, respectively (OR: 0.20, 95% CI: 0.04-0.91, $p=0.04$; OR: 0.22, 95% CI: 0.05-0.92, $p=0.04$).
Conclusions: This study suggested that social and environmental factors rather than drug-related factors have an impact on the resumption of illicit drug use. Harm reduction approach might be more effective than a punishment approach.
Financial Support: Health Labour Sciences Research Grant, Japan

S47. The Influence of Cocaine Use Disorder, Drug Cues and Sex on Decision-Making

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Drug Category Stimulants
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: Cocaine use disorder (CUD) has been characterized as a "disorder of choice". However, prior work has typically not considered choice in dynamic contexts that better represent the uncertainty in real-world decision-making. The present study used probabilistic choice tasks and reinforcement learning models (RLMs) to measure choice dynamics as a function of cocaine use history (CUD vs controls), cue conditions (cocaine cue versus paired neutral cue), and sex.
Methods: Individuals in the CUD (8M, 6F) and control (11M, 10F) groups completed neutral and cocaine-cued tasks (300 trials/task). Trials required a choice between two cues, with responses reinforced according to independent reward probabilities (6:1, 1:6). Each probability ratio was tested in a block of trials and probability changes were not signaled. Following option selection, feedback was provided when a real monetary reward ($0.25) was received or not. Matching analysis modeled choice, and two RLMs, one with and without an exchange rate parameter, represented subjective value of drug-cued choices.
Results: The CUD group demonstrated poorer matching-behavior on the cocaine-cued task than controls ($R2 \pm SEM = 0.59 \pm 0.18, 0.74 \pm 0.17$, respectively). A RLM containing alpha learning, beta temperature, 'c' perseveration, and exchange parameters profiled the CUD group choice behavior during the cocaine-cued task better than other models. Female participants within the CUD group displayed poorer matching-behavior on the cocaine-cued task compared to their male counterparts ($R2 \pm SEM = 0.42 \pm 0.19, 0.71 \pm 0.17$, respectively), chose fewer rich neutral cued options ($M = 63.33 \pm 21.44$, $p = 0.04$), and had a stronger preference for cued images compared to males with CUD.
Conclusions: These results suggest that cocaine cues negatively impact dynamic decision-making in individuals with CUD relative to controls. These data also suggest that females with CUD are more susceptible to cocaine-cue effects in dynamic decision-making.
Financial Support: NIH K01DA043652; NIH R01DA045023

S48. Central Nervous System Activity of Kappa Opioid Receptor Ligands 5'- And 6'-Guanidinonaltrindole

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Drug Category Stimulants
Topic Drug Interactions
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The kappa opioid receptor (KOR) is a promising pharmacological target for the treatment of substance use disorders. In vitro data indicates that 5'-guanidinonaltrindole (5'GNTI) and 6'-guanidinonaltrindole (6'GNTI) are highly potent, selective antagonists and agonists of the KOR, respectively. While both compounds were thought to be peripherally selective, recent in vivo evidence indicates 5'GNTI crosses the blood brain barrier. We sought to further characterize 5'GNTI and 6'GNTI, alone and in combination with the well-characterized KOR agonist U50,488 (U50) and 5HT2A receptor agonist, 2,5-dimethoxy-4-iodoamphetamin (DOI) to better understand the psychomimetic side effects of kappa agonism and KOR selectivity of these ligands.
Methods: Rotarod: Following training on the rotarod apparatus, animals were pretreated with 5'GNTI or 6'GNTI, treated with U50 or saline, and tested at 0, 30, and 60 minutes. Head Twitch: Animals were treated with combinations of DOI, U50, and 6'GNTI or 5'GNTI and total time spent lurching was recorded. Prolactin: Stress minimized mice were pretreated with 6'GNTI, then U50 or vehicle and serum prolactin levels were determined.

Results: Consistent with recent findings, 5'GNTI (30 mg/kg) blocked U50 (20 mg/kg) induced rotarod incoordination. Head Twitch: When U50 (5 mg/kg) was co-treated with DOI (2.5mg/kg), no effect was observed on DOI-induced head twitch, but a lurching behavior was observed that corresponded to the duration of head-twitch behavior. This unique behavior induced by the KOR agonist/5HT2A agonist was blocked by pretreatment with 5'GNTI but not by norBNI. Prolactin: 6'GNTI (30 mg/kg) did not yield prolactin release, while blocking U50 (10 mg/kg) induced prolactin release.
Conclusions: To our knowledge, this is the first report of in vivo work characterizing potentially centrally mediated effects of 6'GNTI. Our results indicate that both 5'GNTI and 6'GNTI cross the blood brain barrier to influence centrally mediated behaviors. Further research is needed elucidate the selectivity of 6'GNTI in vivo.
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S49. Prevalence and Correlates of Active Amphetamine-Type Stimulants (ATS) Use Among Full-Service Women Sex Workers in Malaysia

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Drug Category Stimulants
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: The use of amphetamine-type stimulants (ATS) has been associated with HIV infections and other adverse health outcomes, yet their use among female sex workers (FSWs) in Malaysia has not yet been characterized. Therefore, in the current study, we examined the prevalence and factors associated with active ATS use among FSWs in Malaysia.
Methods: Between February and December 2016, 492 FSWs, including cisgender (n=299) and transgender (n=193) women, were recruited for a cross-sectional study using respondent-driven sampling in Greater Kuala Lumpur, Malaysia. A structured questionnaire was used to collect demographic characteristics, sexual behaviors, ATS and other substance use, behavioral health issues, involvement in criminal justice, and experience of physical and sexual violence. Logistic regression analyses were conducted to determine factors associated with active ATS use, defined as ATS use in the last 30 days.
Results: Nearly one-third of participants (32.3%) reported active ATS use. In the multivariable model, active ATS use was associated with drug use during sex work (aOR=17.10; 95% CI, 8.32-35.15), having moderate to severe level of substance use disorder (aOR=3.38; 95% CI, 1.48-7.70), and engaging in sex work with multiple clients per day (two clients: aOR=3.39; 95% CI, 1.36-8.46; three clients: aOR=5.06; 95% CI, 1.81-14.10).
Conclusions: The results highlight a high prevalence of ATS use and an intersection of ATS use, substance use disorder, and some sexual behaviors that increase the risk of HIV among Malaysian FSWs. Given these findings, prevention and harm reduction strategies need to be tailored to address the increasing use of ATS and the associated adverse health consequences among FSWs in Malaysia.
Financial Support: K01DA051346

S50. Psychosocial and Drug Use Characteristics of Individuals With Stimulant Use Disorder in New York City

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Stimulant Use Disorder (SUD) remains a significant public health concern. Among individuals who use methamphetamine there is a strong association of increased incidence of sexually transmitted infections (STIs) and higher rates of psychological co-morbidities. The aim of the present study was to investigate the

relationship between stimulant use, STIs, and psychosocial functioning among individuals with SUD in New York City.
Methods: Data for this secondary analysis were derived from a clinical trial recruiting amphetamine-type stimulant users (i.e., methamphetamine, non-medical use of prescription amphetamines, or ecstasy) (ClinicalTrials.Gov Registration ID: NCT03226223). Participants completed questionnaires assessing STI history and psychological characteristics [i.e., Connor-Davidson Resilience-Scale-25 (CD-RISC-25), range: 0-100 and the Beck Depression Inventory-II (BDI-II), range: 0-63]. We identified three stimulant groups based on their patters of use: (1) regular methamphetamine users (2) casual methamphetamine users, and (3) non-methamphetamine users who use other psychostimulants. Analyses of variance (ANOVA) were conducted to compare stimulant groups across resilience, depressive symptoms, substance use, and STIs prevalence.
Results: The sample (N=89) was 91% male with a mean age of 34.7 (±8.0). The most common stimulants used within the las year were: ecstasy (89.9%), cocaine (85.4%), methamphetamine (68.5%) and prescription amphetamines (55.1%). Mean BDI-II score was 9.3 (± 9.9), and mean CD-RISC 25 score was 78.2 (± 14.5) with no significant differences across groups. The ANOVA revealed a significant difference ($p < 0.001$) in STI prevalence among the groups: regular methamphetamine users (81.1%) compared to causal methamphetamine users (62.5%) and non-methamphetamine users (21.4%).
Conclusions: These findings suggest that regular methamphetamine users are at elevated risk for STIs compared to other stimulant users, with few corresponding differences in psychosocial functioning. Future studies should further explore the psychological and behavioral factors that put this group at greater risk.
Financial Support: Supported by NIDA grant R21DA040225 to Dr. Jermaine Jones.

S51. Risk of First Episode Psychosis or Mania With Prescription Amphetamine Use

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Drug Category Stimulants
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The aims of this study are to estimate the odds of prescription amphetamine use on the development of first episode psychosis or mania and to determine if there is a dose response effect.
Methods: A case control study using electronic health records was performed in 4,733 patients age 16 – 35 years admitted to McLean Hospital between January 1, 2005 and December 31, 2019. Cases were admitted for an incident episode of psychosis or mania. Controls, matched to cases by year of admission, were admitted for first psychiatric hospitalization without psychosis or mania. We performed multivariable conditional logistic regression to estimate the effect of past month prescription amphetamine exposure on the risk of psychosis or mania, adjusting for age, gender, race, immigration, month of admission, insurance type; smoking, use of cannabis, alcohol, illicit stimulants, sedative/hypnotic drugs, opioids, or hallucinogens; psychiatric diagnoses prior to admit, medications on admission; and family history of bipolar or psychosis. Doses of amphetamine were converted to dextroamphetamine equivalents and divided into tertiles to estimate dose-response effect.
Results: Past month use of prescription amphetamines was associated with an increased odds of psychosis or mania: unadjusted odds ratio (OR) 2.11, 95% CI 1.72 - 2.59; adjusted OR 3.10, 95% CI 2.29 - 4.20. Increased odds of psychosis or mania with prescription amphetamine use was observed for both individuals who were prescribed (adjusted OR 3.05, 95% CI 1.99-6.15) or misused non-prescribed amphetamines (adjusted OR 3.50, 95% CI 2.16-4.30). A dose-response was observed: low dose (≤ 15 mg dextroamphetamine equivalents): adjusted OR 1.79, 95% CI 1.15-2.80; medium dose (>15 mg to ≤ 30 mg): adjusted OR 3.56, 95% CI 2.23-5.69; high dose (> 30 mg): adjusted OR 5.64, 95% CI 3.25-9.77.
Conclusions: Prescription amphetamines are associated with an increased risk of psychosis and mania, with higher doses associated with the greatest risk.
Financial Support: NIMH K23MH110564, R01MH122427.

S52. Treatments for the Fourth Wave: Association of Bupropion, Naltrexone, and Opioid Agonist Therapies With Stimulant-Related Events in Opioid Use Disorder

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: There are currently no FDA-approved medications for the treatment of stimulant use disorders. It is unknown if the recently demonstrated protective effect of bupropion and naltrexone in methamphetamine use disorder holds true in patients with opioid use disorder (OUD) and comorbid stimulant use. It is also unknown whether OUD medications (MOUD) other than bupropion, and antidepressant medications other than bupropion, exhibit protective effects against stimulant use in patients with OUD.
Methods: Using the IBM MarketScan (2006-2016) databases, this recurrent-event, case-crossover study examined insurance claims from 51,084 individuals with OUD. We used conditional logistic regression to compare risk of admission for stimulant-related adverse events associated with exposure to bupropion, selective serotonin reuptake inhibitors (SSRIs), and MOUD (buprenorphine, naltrexone, and methadone). Secondary analyses were conducted by OUD subpopulation (patients receiving vs not receiving MOUD), stimulant type (cocaine; amphetamine) and event type (psychotic events; accidents or poisonings).
Results: Bupropion was associated with a 23% reduction in odds of stimulant-related events (odds ratio [OR]=0.77, 95% CI: 0.72-0.82), as opposed to 10% (OR=0.90, 95% CI: 0.86-0.93) for SSRIs. MOUD was associated with decreased odds of stimulant-related events, with a 33 % reduction for buprenorphine (OR=0.67, 95% CI: 0.64-0.71), 35% for naltrexone (OR=0.65, 95% CI: 0.60-0.70), and 41% for methadone (OR=0.59, 95% CI: 0.51-0.67). These effects were sustained in secondary analyses stratifying by cocaine- and amphetamine-related events, event subtype, and OUD subpopulation.
Conclusions: Our findings show that among persons with opioid use disorder, bupropion and MOUD were associated with decreased risk of admissions for stimulant-related events, with far more modest effects observed for SSRIs. We also observed a robust association between bupropion or MOUD and reductions in both cocaine- and amphetamine-related events, spanning psychotic events, falls, injuries, and poisonings. As there are no FDA-approved medications for the treatment of problematic stimulant use, our results may have significant clinical implications.
Financial Support: NIH R25 MH112473-01, KYX; R21 DA044744, RAG; U10 AA008401, R01 DA036583 LJB; K12 DA041449 CMM

S53. Utilizing a Nonhuman Primate Model to Examine the Importance of Sleep/Wake Architecture in Treating Substance Use Disorder

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Drug Category Stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The goal of the present research is to characterize aspects of sleep quality and architecture in cocaine-naive freely moving young (5-12 year old) male and female cynomolgus macaques and then again after acquisition of cocaine self-administration, throughout maintenance and following potential treatments.
Methods: For this study, we evaluated baseline sleep architecture, defined as the amount of time spent in various stages of sleep, as well as sleep quality, meaning the amount of delta power present during NREM sleep. We recorded from monkeys for 16-24 hours at a time, 12 of which the lights in the room were off. We specifically examined the influence of single- vs. pair-housing and the impact of wearing a primate collar in male (N=4) and female (N=4) monkeys. Female animals were evaluated in both the follicular and luteal phases in order to better evaluate changes in sleep throughout the menstrual cycle.
Results: Sleep disruption is a common aspect of many psychiatric illnesses and has been implicated as a target in finding new pharmacotherapies for substance use disorders. Nonhuman primates are the ideal animal subject for studying sleep due to their similarity to humans regarding duration and stages of sleep

including N1, N2, and N3 stages of non-REM sleep and REM sleep, sleep spindles and K-complexes. This allows for the utilization of nonhuman primates for longitudinal, within-subject design studies evaluating the relationship between quality of sleep and vulnerability, maintenance, and potential pharmacotherapies for substance use disorder.
Conclusions: While the data are still being analyzed, this characterization is necessary for informing us on how future studies will be conducted in order to evaluate sleep using EEG telemetry and how sensitive sleep architecture is in freely moving male and female cynomolgus macaques. Supported by DA017763
Financial Support: Supported by DA017763

S54. Voluntary Exercise Prevents Long-Term Incubation of Cocaine Craving in Female and Male Rats

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Drug Category Stimulants
Topic Treatment
Abstract Detail Animal Study
Abstract Category Original Research
Aim: To compare the effects of voluntary aerobic exercise (AEx) in a running wheel (vs. stationary wheel access) on incubation of cocaine craving in female and male rats.
Methods: The present study compared the effects of voluntary aerobic exercise (AEx) in a running wheel (vs. stationary wheel access) on incubation of cocaine craving in female and male rats over 30 (vs. 3 days) of extinction.
Results: Results indicated that AEx prevented incubation of cocaine craving in females (Zlebnik and Carroll, 2015) in the 30 day, but not the 3-day incubation group. The present study replicated this treatment in male rats with procedures that were identical to those used previously in females (Zlebnik and Carroll 2015). Results indicated that AEx (vs. a stationary wheel control) blocked incubation of cocaine craving in males, with reductions in craving similar to those previously found in females. However, in the present study, AEx also reduced short-term craving in males tested in the 3-day incubation groups, compared to stationary-wheel controls, and effects of AEx on the 3-day abstinence groups in males were similar to those in the 30 day groups. AEx-reduced craving in the 3-day incubated males was not found in the previously-tested females (Zlebnik and Carroll 2015).
Conclusions: Males may be more responsive than females to the effects of AEx on long- and short-term drug craving during abstinence. Overall, results support voluntary, long-term self-initiated and self-sustainable self-treatments (e.g., AEx), to prevent long-term incubated craving that is related to relapse to drug abuse in humans.

S55. Addiction Severity and Language-Based Temporal Perspective in Cocaine Use Disorder

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: A defining characteristic of cocaine use disorder (CUD) is repeatedly choosing present cocaine use over future alternate rewards. Temporal perspective describes one's relative focus on the past, present, or future. Studies measuring temporal perspective using self-report and decision tasks show higher present focus relates to more substance use, while future focus relates to less use. Research shows language samples may offer a convenient and valid measure of temporal perspective. However, the relationship between addiction severity and temporal perspective in CUD has not been assessed using language samples. We hypothesized that higher addiction severity would relate to higher past- and present-focused language and lower future-focused language in individuals with CUD.
Methods: This secondary analysis used baseline data from treatment-seeking adults with CUD (N=32). We measured temporal perspective using word-count-based analysis to calculate percent of words with past, present, and future focus from participant speech during an initial motivational interviewing session.

Addiction severity was assessed through quantity of use (money spent and days of use in past 30 days) and qualitative impact on functioning (CUD symptoms). Using multiple regression, we analyzed temporal perspective (past, present, future) as predictors of addiction severity.
Results: While present and past focus were negatively correlated with each other ($r=-0.74$, $p<0.05$), multiple regression models passed testing for multicollinearity. Analyses revealed no significant relationships between language-based temporal perspective and addiction severity (quantitative: $R2=0.09$, $F(3,28)=0.87$, $p=0.47$; qualitative: $R2=0.01$, $F(3,28)=0.07$, $p=0.97$).
Conclusions: Addiction severity in CUD was not related to temporal perspective, as assessed with a simple language-based measure. It is possible that language measures, particularly from therapy sessions, may show greater utility in predicting outcomes of treatment rather than cross-sectional severity or that more sophisticated language analysis is needed. Qualitative analyses may aid in understanding the negative relationship between present and past focus seen during motivational interviewing.
Financial Support: Supported by K08DA040006 to MCW

S56. Associations Between Prescription and Illicit Opioid and Stimulant Use in the United States, 2015-2019

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Drug Category Stimulants
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Overdose deaths involving opioids and stimulants continue to reach record highs in the United States. While significant attention has been paid to the relationship between prescription and illicit opioid use, little work has focused on the association between prescription and illicit stimulant use. Thus, this study explores the relationships between prescription and illicit stimulant and opioid use.
Methods: We used 2015-2019 nationally representative data from the National Survey on Drug Use and Health. Using adjusted multivariate logistic regression, we estimated the associations between past year prescription stimulant or prescription opioid use and misuse, various demographic characteristics, and past year cocaine, methamphetamine, or heroin use.
Results: From 2015-2019, 10.8 and 5.3 million US individuals annually reported misusing prescription opioids and stimulants, respectively. Individuals who misused prescription stimulants were more likely to be ages 18-25 (44.5%; 95% CI: 42.9-46.1) than individuals who misused prescription opioids (21.1%; 95% CI: 20.2-22.0). Increasing severity of prescription stimulant use (no use, use without misuse, and misuse) was associated with increasing rates of both cocaine and methamphetamine use. Rates of cocaine use (11.6%; 95% CI: 10.7-12.6) were higher among individuals with prescription stimulant misuse compared to prescription opioid misuse (5.9%; 95% CI: 5.3-6.5). Heroin use was more common among individuals with prescription opioid misuse (2.2%; 95% CI: 1.8-2.6) than prescription stimulant misuse (0.6%; 95% CI: 0.5-0.8). However, rates of methamphetamine use among individuals with prescription stimulant misuse (2.2%; 95% CI: 1.8-2.6) did not differ, from individuals with prescription opioid misuse (2.4%; 95% CI: 2.0-2.7).
Conclusions: Prescription stimulant misuse, compared to prescription opioid misuse, was associated with higher levels of cocaine use but not methamphetamine use. Screening for other substance use disorders should be considered among people who report prescription stimulant use or misuse. Additional research is needed to understand the relationship between prescription and illicit stimulant use.
Financial Support: Riley Shearer was supported by NIH MSTP grant T32 GM008244

S57. Causal Association Between Recent Methamphetamine Use and Unsuppressed HIV Viral Load Among People Living With HIV Who Inject Drugs in Hai Phong, Vietnam

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Drug Category Stimulants
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: We assessed the association between recent methamphetamine use and unsuppressed HIV viral load among a cohort of HIV positive persons who inject drugs (PWID) in Hai Phong, Vietnam.
Methods: We recruited PWID from October 2016-October 2018 and enrolled in a 36 month cohort to assess changes in HIV infection and associated risk behaviors. We divided methamphetamine use into three categories based on frequency of use in last 30 days: 0 days (no use), 1-19 days (intermediate), and 20 or more days (heavy). Doubly robust models using inverse probability of treatment weighting (IPTW) were used to measure the relationship between recent methamphetamine use and unsuppressed HIV viral load (≥1000, ≥500 and ≥250 copies/mL) measured during follow-up.
Results: We recruited 791 HIV seropositive PWID; 95% male, average age 39.5 (SD 8.9). At baseline, methamphetamine use in last 30 days was as follows: 57.3 % reported no use, 34.5% reported intermediate use and 8.3% reported heavy use; approximately 18.7% had unsuppressed HIV viral load. In the doubly robust adjusted analysis using IPTW, recent methamphetamine use was associated with unsuppressed HIV viral load (adjusted odds ratio (aOR): 2.13, 95% CI:1.44, 3.14) at 1000 copies/mL. The association remained when evaluating lower HIV viral load cutpoints (500 copies/mL aOR: 1.87; 250 copies/mL aOR: 1.83)
Conclusions: Recent methamphetamine use is associated with unsuppressed HIV viral load among PWID. The results indicate the need for targeted interventions for methamphetamine use with additional studies needed to understand possible biological mechanisms involved in elevated HIV viral load among active methamphetamine users.
Financial Support: This work was supported by grants from NIDA (US) 1R01DA041978 and ANRS (France) 12299. The funding agencies had no role in designing the research, data analyses and preparation of the report.

S58. Elevated Brain Lactate Levels in Female Methamphetamine Users

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Drug Category Stimulants
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: The effects of stimulants such as cocaine and methamphetamine (MA) may present severe acid-base abnormalities (Stevens 1994; Burchell 2000). Likewise, stimulants intoxicated patients are vulnerable to severe lactic acidosis. The current research investigates in vivo brain acidity using proton MRS measurements optimized to assess brain lactate levels in females with MA use disorders.
Methods: We investigated brain lactate levels (indicating brain acidity) in the anterior cingulate cortex (18.75 cc) that is known to be the area of MA toxicity. To date, twenty-one subjects (six MA and fifteen HC females) have been enrolled. All spectra were acquired using semi-LASER PRESS pulse sequence (TR/TE=2000/144ms, VOI=25x25x30mm2, Vector=1024, Average=128, BW=1000Hz), which utilized adiabatic selective RF pulses – frequency offset corrected inversion (FOCI; Duration=6ms, BW=65.9 kHz mu factor=10) to refocus spin echo signal. Correlation analysis was performed between brain lactate levels and Hamilton depression rating scale (HAMD).
Results: The MA-using females had elevated brain lactate levels compared to HC (trend toward significance, p=0.06). The increased lactate levels in MA-using females had a positive correlation with HAMD scores (p=0.05). Our measurement methods of lactate signals at 1.33 ppm are demonstrated to be useful and reliable because the broad bandwidth of FOCI RF pulses significantly reduces chemical shift displacement error and enhances spectral signal to noise ratio from in vivo brain.

Conclusions: Our preliminary in vivo brain metabolite data suggests that MA-using females have elevated brain lactate levels, thus having increased brain acidity, as compared to HC. It has been suggested that therapeutic strategy is to utilize neuronal repair as treatment targets in stimulant addiction. Therefore, pharmacotherapy or other interventions that reduce the brain lactate levels are warranted during MA rehabilitation program. Also, monitoring of brain lactate levels during/after treatment session is recommended.
Financial Support: NIH R01 DA043248

S59. Impact of Ketamine or Propranolol During a Novel Retrieval Session on Cue-Induced Reinstatement of Cocaine Self-Administration in Rats

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Strong drug-associated memories are difficult to disrupt. Recent work has shown that presentation of novel information during memory retrieval may render a drug-associated memory vulnerable to disruption in the presence of amnestic agents. Propranolol is a beta-adrenergic antagonist that has been shown to reduce fear reinstatement. Ketamine has been shown to disrupt drug-associated memories. We hypothesized that propranolol and ketamine would reduce cocaine reinstatement if given during a novel memory retrieval session.
Methods: Rats were trained to self-administer cocaine on a fixed-ratio 1 (FR1) schedule and given a cocaine-reinforced 30 min memory retrieval session on either an FR1 or novel variable-ratio 5 (VR5) schedule or given no retrieval session. Saline (control) or propranolol (10 mg/kg, i.p.) was administered either 30 min before or immediately after retrieval, then lever-pressing was measured during a cue reinstatement session the next day. In the next experiment, saline or ketamine (6 mg/kg, i.p.) was administered 10 min pre-retrieval. The following day, rats were subjected to 30 min of extinction followed immediately by 30 min cue reinstatement.
Results: Post-FR1 retrieval propranolol decreased reinstatement compared to the no retrieval group. Pre- and post- VR5 retrieval propranolol did not affect reinstatement, suggesting that novelty prevented disruption of reconsolidation in these groups. In the ketamine experiment, there was no significant reduction in reinstatement with FR1 or VR5 retrieval, suggesting no impact of ketamine on memory updating.
Conclusions: Propranolol blockade of noradrenergic activity may prevent novelty-induced arousal when using a novel retrieval session, but not when using a familiar retrieval session. Preliminary ketamine results suggest no impact on cue reinstatement when used during either retrieval session.
Financial Support: Washington State University Alcohol and Drug Abuse Research Program (ADARP); NIH DA 040965; and the Good Samaritan Foundation of Legacy Health.

S60. Motivation for Change and Duration of Inpatient Treatment Among Patients With Cocaine Use Disorder

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Drug Category Stimulants
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Motivation for change has been shown to be a predictor of outcome in substance use disorder treatment. Staff nurses at inpatient treatment facilities often observe changes in patient behavior after two weeks of inpatient treatment among patients admitted for Cocaine Use Disorder that suggest a declining motivation for treatment. This decline in motivation is often associated with early discharge. This trial was intended to determine if changes in motivation noted after 14 days of inpatient treatment measured by the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) were associated with early or AMA discharge.

Methods: Patients with Cocaine Use Disorder admitted for inpatient drug rehabilitation were recruited. The SOCRATES was administered to each subject at admission and 14 days later during a scheduled 30 day inpatient treatment program. Change scores on the three subscales were measured. The primary outcome was days of inpatient treatment. The secondary outcome was AMA discharge.
Results: 97 subjects with Cocaine Use Disorder were included. Preliminary results showed that increased or unchanged Ambivalence subscale scores were associated with treatment retention. Among subjects whose Ambivalence score increased or remained same 49 percent remained for 30 days. However, among subjects whose Ambivalence score declined, 24 percent remained for 30 days. Declining ambivalence scores were also associated with an increased rate of AMA discharge.
Conclusions: Preliminary results suggest that reductions in scores on the Ambivalence subscale of the SOCRATES at 14 days were associated with fewer days of inpatient treatment and an increased rate of AMA discharge. Interventions aimed at promoting motivation for change during inpatient drug treatment should be sought. Complete results will be presented at the meeting.

S61. Observed Increase in Methamphetamine Use Risk Among Vietnamese Methadone Patients: 2018-2021 Repeated Surveys

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Drug Category Stimulants
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The global rise of methamphetamine use is threatening the current efforts of HIV and opioid use treatment programs. However, the course of methamphetamine use is not well understood, compared to that of opioid use, especially in countries where methamphetamine use has been newly introduced but rapidly become the first drug of choice. Our study aims to examine (1) changes in prevalence and risk level of methamphetamine use over the 3-year interval among methadone patients and (2) factors associated with increased or decreased risk level of methamphetamine use over time.
Methods: We used data from 2 surveys in 2018 and 2020-2021 on the same 345 patients in 3 methadone clinics in Hanoi. Participants provided their urine drug screens and responded to the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). Of them, 75 who tested positive with methamphetamine or scored 4 or greater on ASSIST in 2018 completed a questionnaire with demographic and comorbidity information. We conducted logistic regression model to explore the factors associated with increased risk level of methamphetamine use.
Results: On the same participants, the prevalence of methamphetamine use decreased from 16.5% in 2018 to 9.3% in 2020-2021. However, the median ASSIST score increases from 0 (IQR: 0-3) to 3 (IQR: 0-6) over time. More participants scored at moderate and high risk in 2020-2021 than in 2018 (22.6% vs. 17.8%). Methamphetamine use risk increased among 40.3% participants and decreased among 15.4%.
Among the 75 participants with demographic and comorbidity data, the factors associated with increased methamphetamine use risk were being single or divorced/separated (OR=4.06, [1.05-20.2]) and testing positive with methamphetamine in 2018 (OR=7.1; [1.1, 46.4]).
Conclusions: The risk of methamphetamine use increased over the 3-year interval among methadone patients in Vietnam. Prompt actions are needed to address the increased severity of methamphetamine use.
Financial Support: NIH R01DA050486

S62. Pilot Study Testing the Feasibility, Acceptability, and Initial Efficacy of a Remote Caffeine Reduction Intervention

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Drug Category Other, Caffeine
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: There is growing recognition that some caffeine users experience caffeine-related problems, however, little research has been conducted to evaluate caffeine cessation treatments. This pilot study examined the acceptability and initial efficacy of a remotely-delivered behavioral intervention to gradually reduce caffeine use over 6 weeks among adults who report caffeine-related problems.
Methods: 36 adults enrolled in the study and received access to a digital manual containing information about caffeine and instructions for gradually reducing caffeine consumption over 6 weeks with no counseling or additional support. Caffeine consumption, sleep, anxiety, gastrointestinal symptoms, and other caffeine-related distress was assessed before treatment, weekly during treatment, and at 7 weeks after receiving the treatment manual (end-of-treatment) using standardized measures. Screening, treatment, and follow-up sessions were completed remotely via HIPAA-compliant video visits and weekly surveys were completed via Qualtrics. Repeated-measures ANOVA tested the effect of the manualized intervention on caffeine reduction and related problems.
Results: Participants reported using an average of 471 mg caffeine at intake. Sleep disturbance was the most reported caffeine-related problem at screening (86%), followed by anxiety (69%) and feeling dependent on or addicted to caffeine (67%). Completers (N=33) reported a significant reduction in caffeine use between baseline and end-of-treatment (421mg vs 111mg, $p<.01$). Significant reductions were also observed on the Pittsburgh Sleep Quality Index (8.9 vs 6.6, $p<.01$), the Generalized Anxiety Disorder-7 (7.3 vs 4.8, $p<.05$) and the Gastrointestinal Symptoms Rating Scale (21.9 vs 12.6, $p<.01$). Study follow-up rate via video visit was high (92%) and participants generally rated the intervention as easy and helpful.
Conclusions: Participants receiving the remote manualized caffeine intervention reported significantly decreased caffeine use and improvements in caffeine-related problems. These pilot findings provide strong initial evidence of the feasibility, acceptability, and initial efficacy of the remote-delivered intervention, which will be further evaluated in a randomized controlled trial.
Financial Support: R01 DA03890

S63. Open Board

S64. Beliefs About Medications for Opioid Use Disorder Among Healthcare Practitioners and Community Stakeholders in Rural New England

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Medications like methadone and buprenorphine are the most effective way to treat people with opioid use disorder (OUD), but most people entering treatment for OUD in the US don't receive these medications, especially in rural areas. This may be due in part to misinformation about and stigma towards medications for OUD (MOUD). Our group has been surveying healthcare practitioners and community stakeholders in rural counties in Vermont, New Hampshire, and Maine as part of a larger effort to identify substance use disorder treatment needs and barriers in these areas. Surveys in all three states included two items that may help assess misinformation about and stigma towards MOUD in these groups.
Methods: We calculated the overall percentage who agreed/strongly agreed with the statement "Medications (like methadone and buprenorphine) are the most effective way to treat people with opioid use disorder" and disagreed/strongly disagreed with the statement "Medications given to treat people with opioid use disorder (like methadone and buprenorphine) replace addiction to one kind of a drug with another." We also compared the percentage of practitioners vs. stakeholders endorsing these responses of interest for each statement.
Results: Overall, a convenience sample of 750 people completed a survey, with 57% agreeing/strongly agreeing that MOUD is the most effective treatment and 52% disagreeing/strongly disagreeing that MOUD replaces one kind of drug with another. Comparisons indicated a significant, twofold-difference in the percentage of practitioners vs. stakeholders agreeing/strongly agreeing that MOUD is the most effective treatment (72% vs. 36%; $p<.001$) and a smaller, but still significant, difference in the percentage disagreeing/strongly disagreeing that MOUD replace one kind of drug with another (59% vs. 43%; $p<.001$).

Conclusions: These results suggest that despite overwhelming evidence of the efficacy of MOUD, some healthcare practitioners and the majority of community stakeholders in rural New England may be misinformed or biased against them.
Financial Support: Health Resources and Services Administration

S65. Body Image Dissatisfaction Among Patients Receiving Methadone Maintenance Treatment

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Although prior studies of patients receiving methadone maintenance treatment (MMT) have documented elevated levels of overweight and disordered eating, none have systematically investigated body image dissatisfaction (BID). We examined BID and its association with important MMT quality indicators: psychological distress and health-related quality of life (HRQoL).
Methods: From 2014-2015, participants (N=164) were recruited from outpatient MMT programs at the APT Foundation, a non-profit community-based organization located in Connecticut. Participants completed self-report measures that assessed treatment characteristics, body mass index (BMI), BID (Body Shape Questionnaire-8), psychological distress (Brief Symptom Inventory-18), and two types of HRQoL, mental and physical (Medical Outcomes Study Short Form 12-Item). General linear models were conducted to test whether BID was associated with psychological distress and mental or physical HRQoL, after controlling for age, gender, race/ethnicity, body mass index, years of regular opioid use, MMT duration, and chronic pain. Analyses were also performed to test whether associations varied as a function of gender.
Results: Women (vs. men) and patients with obesity (vs. normal weight) reported significantly higher BID. Higher BID was associated with higher psychological distress and lower physical HRQoL. BID was not associated with mental HRQoL; however, there was a significant interaction whereby the association between higher BID and lower mental HRQoL was stronger in men than women.
Conclusions: The prevalence of BID in MMT settings may be elevated among women and patients with obesity; however, the association between BID and poorer mental HRQoL may be stronger in men than women. Future prospective research should examine the associations longitudinally between BID and MMT outcomes and quality indicators.
Financial Support: This research was supported in part by funding from the APT Foundation, Inc., and grants from the NIH/NHLBI/NIDA to Dr. Barry (MPI; U01 HL150596-01 and RM1 DA055310).

S66. Characterizing Opioid Withdrawal Experiences Among a Sample of Opioid Using People Who Inject Drugs (PWID)

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Drug Category Opiates/Opioids
Topic Tolerance/Dependence
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid withdrawal symptoms are an extremely salient chronic health condition experienced by opioid using people who inject drugs (PWID), yet little research has documented the consequences of withdrawal among community samples of PWID. This study sought to critically explore opioid withdrawal experiences, the impact of withdrawal on medication-assisted treatment initiation and utilization, and the relationship between withdrawal and infectious disease risk behaviors and overdose.
Methods: Semi-structured interviews were conducted with 30 PWID who self-reported injection opioid use in the prior 30 days (heroin, prescription opioids, opioids in combination with methamphetamine [goofball]

or cocaine [speedball]), in Los Angeles, CA. Topics of inquiry included current drug use, opioid use history, withdrawal pain and severity, coping strategies, and perceptions/access/utilization of medication-assisted treatment (MAT) services. Thematic analysis was used to interpret the transcripts.
Results: Preliminary analysis revealed the following themes: 1) Navigating precipitated withdrawal from buprenorphine and the decision to continue or stop treatment, 2) The influence of social norms and attitudes on buprenorphine interest and use, 3) Managing withdrawal with other substances (alcohol and other illicit drugs), 4) Battling the need to alleviate physiological withdrawal symptoms while recognizing increased overdose risk.
Conclusions: Efforts to improve access to OUD medications within current harm reduction settings could have a significant impact on infectious disease prevention, morbidity, and mortality among PWID.
Financial Support: This work was funded by the National Institute on Drug Abuse (NIDA) [grant number R01 DA046049, Project Official Heather Kimmel, Ph.D.]

S67. Differences in Sociodemographic Profiles and Drug Use Patterns of Individuals With Current Opioid Use Disorder Depending on Opioid Use Preference

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Investigations comparing illicit opioid use preference [e.g., intravenous (IV) vs intranasal (IN) heroin and/or fentanyl] have largely focused on differences in infectious disease comorbidity (e.g., HIV, Hepatitis C). The present study aimed to explore potential differences in sociodemographic factors and drug use patterns between IN and IV opioid users.
Methods: This study is a secondary analysis of data from a recently completed clinical trial that recruited non-treatment-seeking individuals with Opioid Use Disorder (OUD) from the New York City metropolitan area. Participants underwent clinical interviews to quantify individual and drug use characteristics [i.e., length of opioid use, daily intake, time between "hits" (i.e., administrations of opioid(s)), hours until the onset of withdrawal, and use of other drugs]. A bivariate analysis was conducted to identify significant associations as a function of opioid use preference.
Results: Among 58 participants included in the current analysis (27 IV users and 31 IN users), 6% IN users and 15% IV users were female. Mean age was significantly higher among IN users [47.0 (±6.43) years] relative to IV users [39.0 (±9.83) years]. The mean duration of opioid use among IN users, 16.6 (±9.64) years, and IV users, 16.1 (±12.2) years, as well as mean daily morphine equivalent dose for IV (88.0 mg) and IN (73.0 mg) users were not significantly different. African Americans (59%) were more likely IN users and IV users were more likely Caucasian (46%), $p<0.01$. IV users reported waiting longer between "hits", $p<0.01$, in addition to experiencing withdrawal within a shorter period of time [mean 13.0 hours (IV) vs 21.0 hours (IN)], $p<0.03$.
Conclusions: These data suggest that IN and IV users have specific sociodemographic profiles and patterns of use. Future studies should investigate these differences more comprehensively, as they may have important implications for overdose risk and treatment.
Financial Support: Supported by NIDA grant U54DA037842 to Dr. Frances Levin.

S68. Disparities in Opioid Use Disorder Related Hospital Use Among Postpartum Virginia Medicaid Members

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human

Abstract Category Original Research
Aim: We report the prevalence of opioid use disorder (OUD) related hospital use during the year postpartum among Virginia Medicaid members in the years preceding the COVID-19 pandemic. We secondarily assess how prenatal OUD treatment is associated with postpartum OUD-related hospital use. We present outcomes stratified by White and Black non-Hispanic individuals to bring attention to the devastating impacts of the overdose crisis within communities of color.
Methods: This population-level retrospective cohort study used Virginia Medicaid data for live infant deliveries between July 2016 and June 2019. OUD-related hospital use included overdose events, emergency department visits, and acute inpatient stays. Independent variables of interest were prenatal receipt of medication for OUD (MOUD) and other treatment components (e.g., case management, behavioral health). Both descriptive and multivariate analyses were performed for all deliveries and stratified by race (non-Hispanic White, non-Hispanic Black).
Results: The study sample included 97,102 deliveries. Over a third were by Black birthing parents (n=34,742). Prenatally, 2.3% had evidence of OUD, more often among White (3.5%) than Black (0.8%) non-Hispanic birthing parents. Postpartum OUD-related hospital use occurred in 10.8% of deliveries with OUD, more commonly after deliveries by Black, non-Hispanic birthing parents with OUD (18.1%) than their White, non-Hispanic counterparts (9.7%), and this disparity persisted in the multivariable analysis (Black AOR 1.82, 95% CI 1.27-2.60). Postpartum OUD-related hospital events were infrequent for individuals receiving MOUD within 30-days prior to the event. Prenatal OUD treatment, including MOUD, was not associated with decreased odds of postpartum OUD-related hospital use in the race-stratified models.
Conclusions: Postpartum individuals with OUD are at high risk for mortality and morbidity, especially Black individuals not receiving MOUD after delivery. There continues to be an urgent need to effectively address the systemic and structural drivers of racial disparities in transitions of OUD care through the one-year postpartum period.
Financial Support: NIDA award No. K23 DA053507 from the National Institute of Drug Abuse supports Dr. Caitlin Martin. The Substance Use Disorder Prevention that Promotes Opioid Use Recovery and Treatment Act from the Virginia Department of Medical Assistance Services and The Thomas F. and Kate Miller Jeffress Memorial Trust supports Dr. Caitlin Martin, Dr. Peter Cunningham and Xue Zhao. The Addiction and Recovery Treatment Services Program and Substance Use Disorder Prevention that Promotes Opioid Use Recovery and Treatment Act from the Virginia Department of Medical Assistance Services supported Erin Britton and Dr. Peter Cunningham.

S69. Emergency Department Initiated Buprenorphine/Naloxone Intervention for Problematic Opioid Use: Retention Rates and Predictors, and Health Outcomes at 3 and 6 Months

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To evaluate the impact of Emergency Department (ED) initiated buprenorphine/naloxone intervention for opioid use disorder on treatment retention and health outcomes at 3 and 6 months and to identify predictors of retention success.
Methods: Patients presenting at University of Vermont Medical Center ED with indicators of problematic opioid use were eligible for immediate initiation of suboxone/naloxone intervention and guaranteed appointment at the Addiction Treatment Program (ATP) within 72 hours. ATP is a bridge clinic which supervises treatment stabilization and subsequent referral to a long-term treatment provider. Health and treatment assessments including GPRA Client Outcome Measures were performed at intake, 3 months, and 6 months. Logistic regression with split half cross-validation was used to identify predictors of treatment retention. Paired T-tests assessed differences in outcome measures between intake and 3 or 6 months.
Results: From September 1, 2019, 103 patients were enrolled. Nine participants were withdrawn. Follow up contact was made at 3 and 6 months with 78% and 90% of patients, respectively. 56% of patients were retained in treatment at 3 months and 62% at 6 months. The top five predictors at intake of retention were

age, employment status, past 30-day drug/alcohol impact, self-reported energy, past 30 day illegal drug use, past 30 day cocaine/crack and illegal drug use, although collectively these features were not significant compared to a null model potentially due to lack of statistical power. Improvement in health outcomes was observed across a range of variables ($p<0.001$) including 12.25 fewer days using any drug in last 30 days at 3 months and 18.805 fewer days at 6 months.
Conclusions: The program improves retention in treatment above a literature baseline and demonstrates significant improvement in several health outcomes.
Financial Support: SAMHSA 1H79TI081515-01, NIDA 1R21DA049859- 01, NIGMS 2P20GM103644-06, and University of Vermont Health Network Innovation Grant.

S70. Evaluating the Rate of Reversal of Fentanyl-Induced Respiratory Depression Using cNLX-NP, a Novel Long-Acting Naloxone Nanoparticle

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Fentanyl and fentanyl analogs (F/FA) are becoming increasingly common adulterants in counterfeit prescription pills and illicit drugs due to ease of synthesis and small quantities needed for potency, leading to a surge in drug overdoses. Longer-acting therapies are needed as naloxone, the gold-standard opioid antagonist antidote for reversing opioid overdoses, is insufficient to prevent the toxicity associated with re-narcotization caused by F/FAs and. A novel naloxone nanoparticle (cNLX-NP) has been shown to blunt fentanyl-induced respiratory depression out to 48 hours, demonstrating its potential therapeutic benefit. The purpose of this study was to characterize how rapidly cNLX-NP reverses fentanyl-induced respiratory effects.
Methods: Sprague Dawley male rats (n=6/group) were tested on an oximeter for baseline percent arterial oxygen saturation (%SaO2) challenged with 0.1 mg/kg s.c. fentanyl and 15 min later given 10 mg/kg s.c. doses of naloxone, nalmefene, or cNLX-NP and continuously monitored via oximetry for 10 minutes. One week later the experiment was repeated using a 1:1 mixture of naloxone:cNLX-NP as the reversal agent in the rats that previously received naloxone alone.
Results: While both naloxone and nalmefene rapidly reversed %SaO2 to baseline within 1 minute, rats that received cNLX-NP did not return until 10 minutes after administration. Heart rate and breath rates returned to baseline within 1 minute of naloxone and nalmefene but did not return to baseline 10 minutes after cNLX-NP administration. In the group that received naloxone:cNLX-NP, there was a rapid reversal of all fentanyl-induced respiratory depressive effects within one minute.
Conclusions: These results suggest that cNLX-NP alone may not sufficiently reverse F/FA overdose in a timely manner. However, mixing free naloxone with cNLX-NP provided a mechanism to rapidly reverse fentanyl-related effects. Combined, these data support further development of cNLX-NP as a rapid reversal and long-lasting antidote to treat F/FA-induced respiratory depression and overdose, as well as prevent renarcotization in humans.
Financial Support: This work was supported by the National Institutes of Health National Institute on Drug Abuse Grant R21DA050565.

S71. Factors Associated With COVID-19 Testing Among People Who Inject Drugs: Missed Opportunities for Reaching Those Most at Risk

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Drug Category Opiates/Opioids
Topic Health Services

Abstract Detail Human
Abstract Category Original Research
Aim: People who inject drugs (PWID) are vulnerable to SARS-CoV-2 infection. Among PWID in the U.S.-Mexico border region we examined correlates of COVID-19 testing and described encounters with services or venues representing potential opportunities (i.e., 'touchpoints') where COVID-19 testing could have been offered. We hypothesized that PWID with greater touchpoints (e.g., chronic health conditions, recently received health care or been incarcerated) would be more likely to have had a COVID-19 test. We also hypothesized that socio-structural determinant (e.g., food/housing insecurity), COVID-19 disinformation, and COVID-related stigma would be associated with less COVID-19 testing.
Methods: Between October 2020 and September, 2021, 583 participants (74.3% male) aged ≥18 years from San Diego, California, USA and Tijuana, Baja California, Mexico who injected drugs within the last month completed surveys and SARS-CoV-2 serologic testing. Logistic regression was used to identify factors associated with COVID-19 testing prior to enrollment.
Results: Of 583 PWID, 30.5% previously had a COVID-19 test. Of 172 PWID who tested SARS-CoV-2 seropositive in our study (30.1%), 50.3% encountered ≥1 touchpoint within the prior six months where COVID-19 testing could have been offered. Factors independently associated with ≥2-fold odds of COVID-19 testing were living in San Diego (versus Tijuana; aOR=4.52), having recently been incarcerated (aOR=2.72) or attending substance use disorder (SUD) treatment (aOR=2.41) and having at ≥1 chronic health condition (aOR=2.66). Recent homelessness (aOR=1.77), having had at least one COVID-19 vaccine dose (aOR=1.97) and having been tested for HIV or HCV since the pandemic began (aOR=1.52) were also independently associated with COVID-19 testing.
Conclusions: We identified several factors independently associated with COVID-19 testing and multiple touchpoints where COVID-19 testing could be scaled up for PWID, such as SUD treatment programs and syringe service programs. Integrated health services are needed to improve access to rapid, free COVID-19 testing in this vulnerable population.
Financial Support: This work was supported by the National Institute on Drug Abuse (NIDA) (R01DA049644-S1, K01DA043412, T32DA023356 and RADxUP, R01 DA049644-02S2). Additional support was provided by the National Institute of Allergy and Infectious Diseases (P30 AI036214).

S72. Fentanyl's Rising Presence in Oregon's Drug Supply and Knowledge, Attitudes, and Behaviors Among People Who Use Drugs

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Illicitly manufactured (nonpharmaceutical) fentanyl has reconfigured the illicit drug market, contributing to a drastic increase in overdose deaths. Illicit fentanyl, ubiquitous in the Northeast and Midwest, has recently reached the West. For this qualitative study, we explored knowledge, attitudes, and behaviors among people who use drugs (PWUD) in response to the emergence of fentanyl in the drug supply.
Methods: We conducted 34 semi-structured phone interviews with PWUDs in Oregon from May to June 2021. Eligible participants had used illicit drugs in the past 30 days and were age 18 or greater. We analyzed transcripts and constructed themes.
Results: Participants described increased availability of nonpharmaceutical fentanyl and were aware of the adulteration of heroin, pills, and other drugs with fentanyl. Some doubted methamphetamine contamination by fentanyl. Participants feared the increased overdose risk of fentanyl but remained reluctant to call first responders to an overdose emergency because of perceived individual competence to reverse an overdose, fear of law enforcement, and prior negative interactions with healthcare. Some felt that fentanyl preference was irrelevant since fentanyl was unavoidable. Participants reported harm reduction practices including communicating about fentanyl with dealers and peers, testing for fentanyl, using smaller quantities of drugs, smoking instead of injecting, and carrying naloxone. Participants shared ideas to reduce harm from fentanyl:

address stigma, increase access to harm reduction and treatment services, and regulate the drug supply through legalization or providing a safe supply.
Conclusions: PWUD are responding to the rise of fentanyl in the West and are concerned about the increasing uncertainty of the drug supply. They are willing to adopt harm reduction behaviors but remain hesitant to call first responders for an overdose. Increased access to harm reduction and treatment services and addressing stigma are essential to reduce injury and death from nonpharmaceutical fentanyl.
Financial Support: This work was supported by the National Institutes of Health, National Institute on Drug Abuse (UH3DA044831, UG1DA01581), Centers for Disease Control and Prevention (1 NU17CE925018-01-00), and the Oregon Clinical and Translational Research Institute (UL1TR002369).

S73. Frequency of Opioid Response Network Technical Assistance Requests Addressing Substance Use Disorder Stigma

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: The Opioid Response Network (ORN) is a Substance Abuse and Mental Health Services Administration-funded initiative that provides educational resources and training at no cost to states, communities, organizations and individuals. ORN has consultants in all 50 states and 14 US territories, whose expertise covers opioid and psychostimulant use disorders. People who use drugs (PWUD) often have highly stigmatized identities. Due to its corrosive impact on health, stigma is a significant barrier to resolving substance use disorders. Targeting stigma is becoming an increasing focus of organizations that engage PWUD. The purpose of this analysis was to assess if interest in addressing stigma can be found in ORN's technical assistance (TA) requests.
Methods: A data request was submitted through ORN's repository of its TA requests. The data inquiry sought to identify all TA requests (i.e., trainings and symposia) that mention "stigma." The data request covered May 2018 - November 2021. Raw data and pre-specified summaries were provided directly to the first author.
Results: In total, 165 TA requests were identified with a specific mention of stigma; constituting 7.4% of the total requests to date (2,228). In 2018, stigma was specified in 15 requests (3.2% of total), 59 (10.2%) in 2019, 56 (9.9%) in 2020, and 48 (7.3%) in 2021 (to-date). Approximately 69% of stigma-related TA requests targeted unique or hard-to-reach populations; the most common being: criminal justice populations (45% of total requests), people living in rural areas (35%), intravenous users (24%), the uninsured or underinsured (21%), and those experiencing homelessness (19%). Notable differences in geographic distribution of stigma-related requests were also observed.
Conclusions: Research has shown that reducing stigma improves support for public-health approaches for PWUD. These data indicate that stigma is a frequent target within ORN TA requests. However, increasing client awareness of stigma's impact on health and ORN resources may increase their utilization.
Financial Support: The work of the ORN and the preparation of this abstract were funded by a Substance Abuse and Mental Health Services Administration grant (1H79TI083343) to the American Academy of Addiction Psychiatry in collaboration with the Addiction Technology Transfer Center Network, at the University of Missouri - Kansas City, Columbia University Division on Substance Use Disorders and a large coalition of over 40 national professional organizations. Visit OpioidResponseNetwork.org for more information. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

S74. Health-Related Quality of Life in Patients With Opioid Use Disorder Initiating Medication Assisted Treatment in Primary Care

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Medication assisted treatment (MAT) represents the standard of care for patients with opioid use disorder (OUD). Patients with OUD often experience a number of co-occurring issues (e.g., housing instability, interpersonal problems, and medical conditions) that may diminish their quality of life, adherence to MAT, and treatment outcomes. For this reason, clinical guidelines recommend that MAT include both medication and psychosocial treatment. This study examines health-related quality of life (HRQOL) among individuals who have recently initiated MAT.
Methods: Participants were 136 adults enrolled in a randomized, controlled trial testing the comparative effectiveness of two psychosocial treatments delivered in conjunction with buprenorphine-based MAT. Participants completed the Short Form-36, a well-established measure of HRQOL, as a part of the baseline assessment.
Results: Participants in the sample were an average age of 45.1 years (±12.4), the majority identified as Male (68.1%), 30.6% identified as Hispanic/Latinx, and 25.0% identified as Black. Results indicated that participants in the sample reported diminished HRQOL in several domains relative to normative values from individuals with chronic conditions, including role limitations due to emotional problems (M=46.7±45.3), emotional well-being (M=54.8±26.3), social functioning (M=60.1±34.3), and pain (M=52.2±33.3).
Conclusions: Findings from this preliminary study support the recommendation that MAT include both medication and psychosocial treatment as patients initiating MAT for OUD reported low HRQOL in several areas, including social and emotional functioning, that could be addressed through adjunctive psychosocial treatment. Adopting more holistic, person-centered approaches to OUD treatment that includes both medication and evidence-based psychosocial treatments could serve to not only improve patients' quality of life, but also promote their engagement and retention in MAT and overall success in treatment.
Financial Support: This study is funded by the Patient Centered Outcomes Research Institute.

S75. Impact of Anxiety Severity on Retention in Opioid Agonist Therapy: A Secondary Analysis of the Optima Trial

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Drug Category Opiates/Opioids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: The Optimizing Patient Centered-Care: A Pragmatic Randomized Control Trial Comparing Models of Care in the Management of Prescription Opioid Misuse (OPTIMA) trial investigated the differential efficacy and safety of methadone and buprenorphine-naloxone for adults with prescription opiodi use disorder. As buprenorphine-naloxone possesses anti-anxiety properties, we aimed to determine the impact of anxiety on outcomes from the OPTIMA trial.
Methods: Drawing on OPTIMA data, we conducted a secondary analysis to examine if the association between opioid agonist therapy (buprenorphine vs. methadone) and retention in treatment varied by anxiety severity. We considered all randomized OPTIMA participants (n=272). The outcome of interest was three different measures of retention in treatment at week 24. Explored covariates included study site, lifetime heroin use, age, sex, gender, ethnicity, living situation, education, opioid use disorder (OUD) severity, previous OAT, pain severity, and baseline substance use (e.g., opioids, stimulants, cannabis, benzodiazepines, and alcohol). Using logistic regression, we examined the bivariable association between treatment type and retention and each outcome measure, stratified by a Beck Anxiety Inventory score of >=21 vs. <21.

Results: In total, 272 randomized participants were involved in the OPTIMA trial, and constituted the analytic sample. The median sample age was 38 years, and most participants were male (66%0, white *68%), and had prior OAT (56%). At the six-month mark, approximately 39% of the entire sample was retained in treatment, favoring methadone (47%) over buprenorphine-naloxone (31%; p=0.01). Moderate-to-severe baseline anxiety (BAI>=21) was a significant effect modifier for retention in treatment with any OAT at the six-month mark (adjusted odds ratio = 2.62; 95% CI, 1.18-5.84) after adjustment for other covariates.
Conclusions: Baseline anxiety severity appears to be associated with retention in treatment with OAT for adults with prescription opioid use disorder and may be associated with an improved response to treatment with buprenorphine.
Financial Support: Dr. Bahji reports research grants from the National Institutes of Health/National Institute on Drug Abuse (NIDA) [R25-DA037756, R25DA033211] through the International Collaborative Addiction Medicine Research Fellowship and the Research in Addiction Medicine Scholars Program through Boston University School of Medicine. In addition, Dr. Bahji is a recipient of the 2020 Friends of Matt Newell Endowment from the University of Calgary Cumming School of Medicine. Dr. Bahji also received financial support from a 2020 Research Grant on the Impact of COVID-19 on Psychiatry by the American Psychiatric Association and the American Psychiatric Association Foundation.

S76. Impact of COVID-19-Related Health Care Disruptions and Regulatory Changes on Nationwide Access to Buprenorphine

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: This study seeks to understand the impact of COVID-19-related health care changes on access to buprenorphine (BUP) nationwide.
Methods: We used IQVIA LRx, a longitudinal prescription dataset with >90% of all dispensed US prescriptions, to conduct an interrupted time series analysis, using the month of March 2020 as our interruption. We included all BUP prescriptions from 2/23/19 to 4/2/21. The outcome of interest was total milligrams (MG) of BUP available per week nationwide, in order to account for prescriptions of differing length. Segmented regression analysis was used to report a change in BUP prescribing compared against baseline trends at 1, 26, and 52 weeks post-initial pandemic period. We also evaluated changes in treatment disruptions (>=28-day gap in days supplied) over time in previously stable patients, defined as 6 months of BUP prescriptions without a disruption.
Results: A total of 31,801,061 prescriptions were included for analysis. While the number of patients with an active BUP prescription each week did not change significantly from expected at 52 weeks, the number of filled prescriptions decreased (-4.4% [95% CI -5.9, -2.9]), the mean number of MG per claim increased (6.1% [5.1, 7.2]), and the mean days supplied increased (6.3% [5.4, 7.3]). The total MG of BUP per week was 1.2% (0.48, 1.9) higher that would be expected from baseline trends ($p<0.001$ for both level and trend changes). Stably-treated patients saw a significant decrease in treatment disruptions at 52 weeks post-initial pandemic period (-28.4% [-33.7, -23.0]).
Conclusions: Following the initial COVID-19 pandemic period, patients received longer prescriptions of BUP, leading to increased MG per claim, and overall increased total MG BUP. Stably-treated patients also experienced fewer treatment disruptions. Regulatory changes around BUP prescribing appear to have helped patients maintain access to medication during the early pandemic period.
Financial Support: 3UG1DA049436-03S1

S77. Long-Term Mortality Among Hospitalized Medical Patients Seen by a Substance Use Disorder (SUD) Consultation Service

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Drug Category Opiates/Opioids

Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: The Navigation Services to Avoid Rehospitalization (NavSTAR) study showed that augmenting a hospital-based SUD consultation service with post-discharge patient navigation reduced hospital readmissions compared to usual care. In the current study, we examined long-term mortality among participants in the NavSTAR trial.
Methods: Participants were adult medical/surgical hospital patients with comorbid opioid, cocaine, and/or alcohol use disorder (N=400; 43% female, mean age=45) who were seen by the hospital SUD consultation service and randomized to Patient Navigation (continued for 3 months post-discharge) or Usual Care. A death certificate search was conducted through an agreement with the Maryland Division of Vital Records, covering 3.3-5.5 years post-enrollment. Baseline prognostic variables spanning sociodemographic and SUD, medical, and mental health characteristics were examined using log-rank tests of survival functions and multivariable proportional hazards Cox regression.
Results: One-third (33.5%) of participants died during the observation period. Overdose or intoxication was listed as a direct or precipitating cause in 43.3% of deaths. There were no significant differences in survival between Patient Navigation and Usual Care arms (HR= 0.85 [0.60, 1.21]; p=0.37). Survival function comparisons showed fewer than expected deaths among participants initially hospitalized with infection (p=0.01), cardiac problems (p=0.01), and comorbid cocaine use disorder (p=0.04), and more than expected among participants with comorbid schizophrenia (p=0.003). In multivariable Cox regression, older age (HR=1.03 [1.01, 1.05]; p<0.001) and schizophrenia (HR=3.43 [1.51, 7.81]; p=0.003) were associated with death, while initial hospitalization for infection was associated with lower risk of death (HR=0.61 [0.38, 0.98]; p=0.04). No other prognostic variables examined were associated with mortality.
Conclusions: Hospital patients with comorbid SUD have high mortality. Relatively few baseline prognostic factors could differentiate survival in this sample. A short-term Patient Navigation intervention, shown effective in reducing readmissions, did not impact long-term mortality. Extended interventions are needed to address the needs of this high-risk population.
Financial Support: NIDA R01DA037942

S78. Modelling Buprenorphine Mitigation of Fentanyl-Induced Respiratory Depression

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: To characterize buprenorphine-fentanyl interaction at the mu-opioid receptor and assess the ability of buprenorphine to reduce respiratory depression associated with escalating doses of fentanyl.
Methods: 14 opioid-naïve healthy volunteers (HVs) and 8 opioid-tolerant (OT) participants (using ≥90 mg oral morphine equivalents daily) received, on 2 separate occasions, intravenous placebo and buprenorphine infusion targeting plasma concentrations of 0.2 or 0.5 ng/mL in HVs and 1, 2 or 5 ng/mL in OT participants. Upon reaching target concentrations, participants received up to 4 escalating intravenous bolus doses of fentanyl (HV: 0.075–0.35 mg/70 kg; OT: 0.25–0.70 mg/70 kg). In an optional third session, HVs received buprenorphine infusion alone. Minute ventilation was measured under isohypercapnic conditions and serial blood samples were collected to measure buprenorphine and fentanyl plasma concentrations. The pharmacodynamic interaction of fentanyl and buprenorphine was characterized by population pharmacokinetic/pharmacodynamic modeling (nonlinear mixed-effects modeling).
Results: Minute ventilation data were well described by receptor association/dissociation models combined with biophase equilibration models. In line with observations, modeling showed that OT participants were less sensitive to the respiratory effects of buprenorphine and fentanyl and that sustained buprenorphine plasma concentrations ≥2 ng/mL markedly reduced the magnitude of respiratory depression and probability of apnea after fentanyl administration in this population. Simulation studies in OT participants investigated the effects of a larger range of fentanyl doses (0.05–5 mg/70 kg) representing clinical fentanyl use and

unintentional overdose. Best clinical outcomes were observed at buprenorphine concentration of 5 ng/mL for the highest dose of fentanyl simulated (5 mg/70 kg).
Conclusions: These analyses describe a second mechanism through which buprenorphine may reduce opioid overdose deaths. When buprenorphine receptor occupancy is sufficiently high, fentanyl can only activate a limited number of receptors and consequently will not cause additional respiratory depression beyond the milder respiratory effects of buprenorphine.
Financial Support: Indivior Inc.

S79. New Federal Guidelines for Buprenorphine DEA-30 Patient Waivers: Will the States Support?

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: The Department of Health and Human Services (HHS) announced new buprenorphine practice guideline exceptions (i.e., removal of the waiver training requirement and attestation to refer to counseling/ancillary services as needed) for obtaining a 30-patient limit DEA waiver in April 2021. The purpose was to increase the number of buprenorphine providers available to treat opioid use disorder (OUD). This study, part of the HEALing Community Study, evaluates whether existing state regulations and statutes will allow for buprenorphine practice without completion of the waiver training (WT).
Methods: We searched Westlaw for buprenorphine regulations and statutes in all 50 states and the District of Columbia (DC) using the term "buprenorphine" and filter terms "SAMHSA", "training", and "waiver". Two researchers independently reviewed the resulting documents and coded each state as requiring WT, requiring WT under some circumstance, or not requiring WT. Answers were logged for each type of waiver-eligible provider (i.e., physicians, physician assistants, and advanced practice nurses). Mentions of "special" training were counted as WT.
Results: The search yielded 151 regulations and 72 statutes. Preliminary results as of October 2021 showed 18 states and DC had no buprenorphine regulations to review. Among the remaining 32 states with buprenorphine regulations, seven had waiver training (WT) requirements, and they varied by practitioner type. Three states required WT for physician assistants (CA, KY, ME), and four states required WT for nurse practitioners (CA, KY, ME, NM), and seven states required WT for physicians (AL, CO, KY, LA, NM, ME, UT). Some of these requirements only apply in certain conditions (e.g., in office-based settings).
Conclusions: Some waivered providers may not be able to practice under current state law without completing the WT. This highlights a mismatch between state and federal policy that may limit the intended expansion of the provider workforce needed to effectively address the ongoing opioid epidemic.
Financial Support: This research is supported by the National Institutes of Health through the NIH HEAL Initiative under award number UM1DA049406 and the Substance Abuse and Mental Health Services Agency under award number H79TI083283. Opinions expressed are those of the authors and do not represent the position of the National Institute on Drug Abuse or SAMHSA. The authors have no relevant conflicts of interest to report.

S80. Opioid Agonist Treatment for Prescription Opioids Dependence: An Updated Systematic Review and Meta-Analysis

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: There are ongoing concerns regarding prescription opioid dependence. This study aimed to assess the effects of maintenance opioid agonist pharmacotherapy for the treatment of pharmaceutical opioid dependence.
Methods: The search included the seven databases. We included randomised controlled trials examining maintenance opioid agonist treatments that compared: 1. Full opioid agonists versus different full opioid agonists or partial opioid agonists for maintenance treatment, and, 2. Full or partial opioid agonist maintenance versus non-maintenance treatments. We used standard Cochrane methodological procedures for study selection, reporting and analysis.
Results: We identified eight randomised controlled trials that met inclusion criteria (709 participants). We found low quality evidence from three studies of a difference between methadone and buprenorphine in favour of methadone on self reported opioid use (risk ratio (RR) 0.49, 95% confidence interval (CI) 0.28 to 0.86), and low quality evidence from four studies finding a difference in favour of methadone for retention in treatment (RR 1.21, 95%CI 1.02 to 1.43). We found low quality evidence from three studies of no difference between methadone and buprenorphine on substance use measured with urine drug screens (RR 0.81, 95%CI 0.57 to 1.17), and moderate quality evidence of no difference in days of self reported opioid use (mean difference 1.41 days, 95% CI 3.37 lower to 0.55 days higher). We found low quality evidence from four studies favouring maintenance buprenorphine treatment over non-opioid treatments in terms of fewer opioid positive urine drug tests (RR 0.66, 95% CI 0.52 to 0.84). There was moderate quality evidence from four studies favouring buprenorphine maintenance over non-opioid treatments on retention in treatment (RR 3.02, 95% CI 1.73 to 5.27).
Conclusions: On the outcomes of retention and self-reported substance use some results favoured methadone over buprenorphine. Maintenance treatment with buprenorphine appeared more effective than non-maintenance treatments. Further data may change these conclusions.
Financial Support: NHMRC Research Fellowships 1163961 and 1135991

S81. Opioid and Alcohol Inpatient Treatment Admissions During the COVID-19 Pandemic

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: In March 2020, the US declared a public health emergency in response to the coronavirus (COVID-19) pandemic and implemented social distancing measures that impacted residential medical facility operations. The association between the COVID-19 pandemic and substance use disorder (SUD) treatment admission rates is unclear. The aim of this research is to assess changes in patterns of Opioid Use Disorder (OUD) and Alcohol Use Disorder (AUD) inpatient admission rates before and during the COVID-19 pandemic.
Methods: Using electronic health records data from two Henry Ford Health System inpatient SUD treatment facilities in southeast Michigan, we performed a retrospective analysis of patients admitted with OUD and AUD from March 1–August 31, 2019 (pre-COVID) and the same 6 months of 2020 (start of the COVID-19 pandemic) and 2021. ICD-10 SUD codes were used to categorize admissions.
Results: Due to the COVID-19 pandemic, both facilities reduced admission capacity by 50% (beginning March 20, 2020). Total SUD admissions across both facilities, within the 6 months of 2019, included 25% OUD (263) and 65% AUD (678) patients. In 2020, admission rates slightly dropped to 23% OUD (91) while the rate of AUD admissions increased to 70% (283). In 2021, admission rates of OUD patients further significantly decreased from 2019 (15%, 110) and significantly increased for AUD (75%, 537). A chi-square test revealed a significant increase in AUD admission rates and a significant decrease in OUD admission rates between 2019-2021, $\chi^2(2)=64.09$, $p<0.01$). There were no between-center differences.
Conclusions: OUD admission rates within two southeast Michigan inpatient treatment centers (one rural and one metropolitan) decreased from 2019 to 2020 and did not recover in 2021, while 2019-2021 AUD rates increased. Substance availability, stress, social isolation, and other factors may account for this COVID-associated change in SUD treatment admission patterns.

Financial Support: National Heart, Lung, and Blood Institute 1U01HL150551 awarded to Mark K. Greenwald, Ph.D. and Timothy A. Roehrs, Ph.D.

S82. Preliminary Findings From a Tool for Calculating the Effects of Replacing High Dead Space Syringes in Naloxone Kits With Reduced Dead Space Alternatives

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Harm reduction programs (HRPs) in the United States distribute over 1-million vials of injectable naloxone annually in kits that typically include instructions, two 1-mL vials of naloxone, and two 3-mL high dead space syringes (HDS). These syringes waste 10% of a naloxone vial in the dead space. We examined the impact of replacing current HDS with reduced dead space (RDS) syringes in naloxone kits.
Methods: We obtained estimates of the wholesale prices of injectable naloxone, HDS needles and syringes currently in kits, and RDS replacements. We extracted dead space measurements from our dead space database and input values into our naloxone waste calculator to compute the impact of different syringe designs on the numbers of naloxone kits distributed and weight of naloxone injected.
Results: HDS syringes in naloxone kits cost $0.10 each and waste 100 µL. RDS syringes with an extended plunger (RDS1) cost $0.09 and waste 50 µL. Syringes with RDS needles (RDS2) cost $0.13 and waste 22 µL. RDS syringes with permanently attached needles (RDS3) cost $0.25 and waste 3 µL. We assumed naloxone cost $5 per vial and organizations distributed 10,000 kits. Compared with HDS, RDS1 would result in 18 more kits distributed and 3,600 mg more naloxone injected: RDS2 would result in 59 fewer kits distributed and 3,800 mg naloxone more injected; RDS3 would result in 294 fewer kits distributed and 3,871 mg more naloxone injected.
Conclusions: A naloxone waste calculator and syringe dead space database could inform HRPs decision-making regarding syringes to include in naloxone kits and potentially increase their effectiveness. With increased presence of fentanyl and the current naloxone shortage it may be prudent to reduce naloxone waste. Additionally, administering a full dose of naloxone could help offset any loss of potency when using a vial of naloxone that has expired.

S83. Prescription Drug Monitoring Program and the Opioid Use Disorder Cascade of Care Model: Opportunities for West Virginia

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Utilizing Prescription Drug Monitoring Program (PDMP) data from the state of West Virginia, the primary aim of the study is to assess linkage and retention in care to understand opportunities for intervention focused on improving outcomes for individuals with OUD.
Methods: For this analysis, WV PDMP data was used to identify buprenorphine prescriptions for treating opioid use disorder. The overall sample included 33,104 individuals of both sexes over a two-year period between 2018-2019 and the subset sample utilized for assessing retention contained 10,026 individuals. Retention was evaluated using the HEDIS measure of 96%, which equates to treatment engagement for 173 out of 180 days. Chi-squared analyses and T-tests were used to examine the difference between those who reached HEDIS retention versus those who did not. Logistic regression analyses were conducted using SAS 9.4 software
Results: Prescriber characteristics: Of the 1,961 providers, the majority were out of state (64%). In-state providers, however, treated the majority of patients in the sample with an average 33.7 (SD: 59.7) patients

vs. 7.4 (SD: 18.6) for out of state providers. Prescription characteristics: The predominant initial dose was 8mg (55.3), and the most common initial day supply of medication was for <7 days (32.3) and 7 days (35.1%) for the subset. Retention at 6 months per the HEDIS measure for the subset sample was 24.5%. Age was considered to be a significant factor with an odds ratio of 1.01 (1.00—1.01) and a p-value of 0.009. Prescribed day supply was also considered significant; for each one day increase in supply, patients were 1.03 times more likely to reach retention.
Conclusions: The findings from this analysis showed that we need to leverage the opportunity of MOUD initiation and focus efforts on increasing retention rates to produce the documented benefits for individuals with OUD and HIV or HCV.
Financial Support: HRSA-038

S84. Preventing Opioid Relapse Among American Indian Women: A Community Based Participatory Approach to Develop a Facebook Intervention

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Program Descriptions
Aim: The opioid epidemic is a major public health problem that disproportionately affects Native communities. While gender-specific risk factors for opioid relapse in women have been identified (e.g., perceived stress, social support), gender-specific interventions for Native women do not exist. We describe a community-based participatory research (CBPR) approach to develop a moderated Facebook group intervention for reducing opioid relapse among Native women.
Methods (Optional): The study concept was designed with Native community partners in Minnesota. A community advisory committee (CAC) was formed to guide all project activities. The CAC is comprised of 11 members, including health care providers, Native community partners, and American Indian women with lived experience. At the advice of our CAC, a Native Elder woman named the study to have meaning in the community beyond the project.
Results (Optional): The name given to the study by the Elder is Wiidookaage'win, an Ojibwe word that means "the place of help, the time of helping." During two meetings with our CAC, potential Facebook moderator postings were designed and iteratively refined to incorporate content (text, images, and videos) consistent with Native American culture and values. Key intervention content domains include the role of stress/trauma on substance use, mindfulness techniques, recognizing and responding to substance use triggers, and links to community resources to support opioid recovery. The CAC also helped to develop study methods.
Conclusions: A CBPR approach was essential to co-create culturally relevant content for the intervention and to name the study, ensuring meaning and recognition in Native communities. Next steps are to conduct qualitative work and beta-testing of the intervention. Consistent with the cultural value of interdependence, social media-formed groups to prevent opioid relapse could lead to greater adoption and sustainability by encouraging collaborative efforts across generations of Native women and leveraging community resilience for coping with stress.
Financial Support: National Institute on Drug Abuse, Clinical Trials Network

S85. Proximity to Treatment and Post-Release Treatment Engagement Rates Among Adults Who Participated in a Comprehensive MOUD Program at the Rhode Island Department of Corrections, 2016-2018

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Providing access to medications for opioid use disorder (MOUD) in carceral facilities is an ethical imperative that provides significant benefits, including greater post-release retention on MOUD and fewer post-release overdose deaths. However, environmental factors, such as proximity to treatment, may impact post-release MOUD access and utilization. Controlling for sociodemographic and clinical factors, this study examined whether geographic proximity to treatment relates to MOUD treatment engagement rates following participation in a comprehensive MOUD program in a carceral facility.
Methods: Drive-times from release locations to nearest opioid treatment programs (OTPs) were calculated for comprehensive MOUD program participants (N=1,160) at the Rhode Island Department of Corrections from December 2016 through 2018. One-way ANOVAs and Kruskal-Wallis tests evaluated drive time differences between sociodemographic groups. Unadjusted and adjusted odds of MOUD treatment engagement in the community at 30-days post-release were calculated and stratified by urban/suburban status using drive-time to nearest OTP as the independent variable; covariates included type of medication taken while incarcerated, induction versus continuation of MOUD while incarcerated, sex, age, and educational attainment.
Results: Drive-time to nearest facility varied by age, race/ethnicity, and educational attainment. Outside of large cities, living within 5-10 (aOR=0.39), 15-20 (aOR=0.47), or 20-40 (aOR = 0.31) minutes was associated with lower adjusted odds of post-release MOUD engagement than living very close (i.e., within 5 minutes). Within large cities, living at drive-time increments between 0-2 and 3-9 minutes away were consistently associated with greater adjusted odds of treatment engagement than living 9-10 minutes away, controlling for all other covariates.
Conclusions: In addition to medication type and prior history of MOUD, proximity to OTPs may relate to MOUD engagement during a high-risk period for opioid overdose after release from incarceration.
Financial Support: This work was supported by the National Institutes of Health [U01 DA050442-01], awarded to Dr. Rosemarie Martin.

S86. Readmission and Comorbidities Associated With Patient-Directed Discharges Among Surgical Patients With and Without Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Among surgical patients with patient-directed discharges ("against medical advice;" PDDs), we determined whether patients with opioid use disorder (OUD) had a higher and/or distinct comorbidity burden and higher readmission rates than patients without OUD. We hypothesized that patients with OUD would have a higher and distinct comorbidity burden and higher rates of readmission.
Methods: Using cross-sectional 2015-2016 data from patient discharge summaries and 448 hospitals in California, Florida, New Jersey, and Pennsylvania, we described differences in patients with and without OUD who had a PDD using ANOVAs, chi-squared tests, and t-tests.
Results: Over 20% (948/4,649) of surgical patients with a PDD were readmitted within 30 days. Nearly 10% (454/4,649) had OUD. Patients with compared to without OUD were younger (mean age=40.2 vs 60.5; P=<0.001) and more often insured by Medicaid (53.8% vs. 27.2%; P<0.001). They more often underwent general surgery (53.5% vs. 35.0%) and less often orthopedic (40.3% vs. 49.2%) or vascular (6.2% vs. 15.8%) surgery (P<0.001). Patients with and without OUD had a similar number of comorbidities (3.1 vs. 2.9; P=.0569). Patients with OUD less often had congestive heart failure (2.4% vs. 6.3%; P=0.001), complications from diabetes (8.4% vs. 15.8%; P<0.001), and hypertension (28.0% vs. 57.9%; P<0.001), yet more often had co-occurring liver failure (15.2% vs. 7.1%; P<0.001), alcohol abuse (14.8% vs. 10.9%; P=0.015), psychoses (16.7% vs. 7.1%; P<0.001) and depression (16.7% vs. 10.5%; P<0.001). A similar

proportion of patients with OUD compared to without OUD (26.3% vs 21.2%; P=0.15) were readmitted within 30-days.
Conclusions: Surgical patients with a PDD and OUD were younger, more often insured by Medicaid, and had distinct comorbidity profiles and surgery types than those without OUD. Patients with a PDD are at high risk of readmission, regardless of whether they have OUD. Avoiding PDDs is important so that patients can receive needed acute care and avoid readmissions.
Financial Support: Funding was received from the National Institute on Drug Abuse (F32-DA053763, French PI), the National Institute of Nursing Research (T32-NR0714, Aiken, PI; R01-NR014855, Aiken, PI), the International Nurses Society on Addictions (French, PI), and the University of Pennsylvania's Office of Nursing Research (French, PI).

S87. Recent Opioid Use Impedes Range Adaptation in Reinforcement Learning in Human Addiction

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Drugs of abuse are potent reinforcers which can seize value-based decisions by overshadowing other reinforcing outcomes, but the underlying mechanisms for this process remain unknown. Recent evidence indicates value-based decisions depend not on the objective (absolute) reward values of choice options but on rescaled values with respect to the range of available reward in a given context, a process of 'range adaptation' that permits fine-tuned representation of value and choice. Here we tested whether range adaptation could explain how opioid exposure and craving/withdrawal states alter decision-making in opioid use disorder (OUD).
Methods: N=38 OUD (n=15 opioid-positive) and N=42 matched controls completed a two-phase reinforcement learning task designed to induce robust context-effects. Participants first learned by trial-and-error the expected values of pairs of cues in two contexts: with either wide or narrow reward range. During transfer, cues were rearranged to create new pairs. No additional feedback was provided, forcing participants to extrapolate cue values from the learning phase which, if learned using range adaptation, could lead to choice errors in some cases. Computational modeling was used to evaluate the latent process engaged during learning, testing for evidence of absolute vs. range-adapted representations of value.
Results: Controls and opioid-negative OUD chose the higher value cues equally well in the wide and narrow reward contexts ($p<0.01$-vs-chance) and made systematic choice errors during transfer ($p<0.05$-vs-chance)—both indicative of range adaptation. By contrast, opioid-positive OUD performed better in the wide context ($p=0.05$-vs-narrow) and, across OUD, those reporting increased withdrawal made fewer transfer errors ($r=0.39$, $p=0.026$), more consistent with encoding absolute-values. Modeling confirmed most controls and opioid-negative OUD (~75%), but only 53% of active users, were better fit by range-adapted (vs. absolute-value) RL models.
Conclusions: Opioid use and associated states impede range adaptation during value-based decision-making, making choices between smaller (typically non-drug) rewards harder when the drug is available.
Financial Support: This work is supported by NIH/NIDA (R01DA053282, R01DA054201).

S88. Relative Risk of Opioid-Involved Death Following Exposure to Treatments for Opioid Use Disorder, Connecticut, 2017

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human

Abstract Category Original Research
Aim: The impact of different treatments for opioid use disorder (OUD) on the risk for an accidental and undetermined opioid-involved overdose fatalities (OOF) remains unclear. To assess this risk, we linked datasets generated by Connecticut state agencies.
Methods: We obtained data on OOD during 2017 from the Office of the Chief Medical Examiner. We obtained individual-level treatment data in the six months prior to the fatal event for medications for OUD (MOUD) dispensed by opioid treatment programs and non-medication-based treatments from the Department of Mental Health and Addiction Service (DMHAS). We used individual-level data from the state's prescription drug monitoring program for office-based buprenorphine receipt.
Results: The 1128 OOFs were linked to the treatment data. In the six months prior to the OOF, 75 decedents had received methadone, 94 had received buprenorphine, and 194 had received non-medication treatment. To determine relative risk, we calculated the number of individuals statewide who received methadone, buprenorphine or non-medication-based treatment during 2017 using data from DMHAS and the DEA's Automation of Reports and Consolidated Orders System (ARCOS). We assumed 80% of individuals with OUD were not receiving treatment at any given moment. Using no exposure to treatment as the referent, the relative rate of OOF was 0.404 (95% CI: 0.320, 0.512) for methadone, 0.603 (95% CI: 0.488, 0.746) for buprenorphine, and 1.568 (95% CI: 1.342, 1.830) for non-medication-based treatment. We conducted sensitivity analysis varying proportion of individuals who did not receive treatment between 15% and 25%, and in all cases no treatment exposure had a lower risk than exposure, in the six months prior to death, to non-medication-based treatment.
Conclusions: These findings suggest that exposure to treatment with methadone and buprenorphine was effective in protecting against OOF, while non-medication-based treatments, as a group, fared worse than no treatment at all.
Financial Support: FDA

S89. Risks of Overdose Events for Patients Undergoing Opioid Use Disorder Treatment

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Patients with opioid use disorder have an increased risk of experiencing an overdose event. While medication for opioid use disorder (MOUD) treatment decreases overdose risks, a quantitative assessment of overdose risk is not presently available. Adverse events including both fatal and non-fatal overdose events are surveyed in pragmatic clinical trials, allowing a more precise estimate of risk of overdose events during MOUD treatment.
Methods: We harmonized the adverse event logs with case report forms in 3 large randomized controlled MOUD clinical trials (CTN-0027, methadone vs. buprenorphine, CTN-0030, buprenorphine for prescription opioid users, and CTN-0051, buprenorphine vs. extended-release naltrexone) from the National Drug Abuse Clinical Trials Network (CTN) (N=2,197). We compared the overall risk for each of the treatment groups (methadone, buprenorphine and extended-release naltrexone) in an intent to treat analysis using survival analysis, making adjustments for differences in the cohort.
Results: 39 overdose events were observed in the 24 weeks after randomization. Overall, assignment to extended-release naltrexone (N=283) was associated with an increased point estimate of risk of overdose event at 24 weeks (6.63%) compared to methadone (N=528, 1.86%) and buprenorphine (N= 1,386, 1.68%) (P=0.0017 Wald Chi-Sq). Self-reported use of benzodiazepine was associated (P= 0.001) with increased risk in all 3 groups (methadone 4.54%, buprenorphine 3.4%, and extended-release naltrexone 13.94%). Being inducted on extended-release naltrexone was associated with a lower risk of overdose (N=204, 3.92%) compared to the never-inducted group (N=79, 8.86%). Sensitivity analyses using competing risk models and time-varying covariates for medication compliance did not alter the findings.

Conclusions: Patients undergoing treatment for MOUD have a substantial risk of overdose events in the first 24 weeks of treatment, possibly higher for those who were assigned extended-release naltrexone and those reported using benzodiazepine at baseline.
Financial Support: NIDA 5UG1DA013035 HEAL INITITIVE SUPPLEMENT

S90. Running to Stand Still: Exaggerated Aversive Salience in Individuals With Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: Using drugs to avert negative consequences of withdrawal may be driven by exaggerated salience of aversive signals (feeling "bad"). Individuals with substance use disorders often show increased insula and ventral striatum activation to drug cues but attenuated activation of these regions to other emotional stimuli. We hypothesized that individuals with opioid use disorder (OUD) would report higher negative affect and pain sensitivity but show lower insula and ventral striatum signals while processing negative stimuli than healthy controls (CTL).
Methods: Two participant groups from a large study on transdiagnostic mental health (Tulsa 1000 study), OUD (n=33, 48% female) and CTL (n=30; 53% female), were compared on (1) depression, anxiety, pain, and urgency questionnaires; (2) a cold pressor task; and (3) a monetary incentive delay (MID) task involving anticipation of small and large gains and losses during functional magnetic resonance imaging. Sex differences were also explored.
Results: OUD reported higher rumination ($p<.001$; $\eta^2=.36$), anxiety sensitivity ($p<.001$; $\eta^2=.33$), negative urgency ($p<.001$; $d=2.10$), and pain interference ($p=.04$, OR=2.87) than CTL. Two additional trends emerged, wherein (1) OUD exhibited faster time to peak pain on the cold pressor task than CTL ($p=.06$, $\eta^2=.06$), as well as lower anterior insula signal ($p=.07$, $d=0.43$) across MID loss anticipation conditions (no, small, large); and (2) a group by sex by condition interaction, indicating that OUD women showed lower ventral striatum signal than CTL women when anticipating small and large MID losses ($p<.03$, $d=.89$-$.95$).
Conclusions: Conclusions: Findings provide partial support for the hypothesis that individuals with OUD show exaggerated aversive salience. However, attenuated brain responses to potential negative consequences were only observed in women. Small sample sizes and a cross-sectional design warrant replication. A longitudinal study by our research group is underway to identify how these metrics predict and track OUD recovery.
Financial Support: R01DA050677 (PI: Stewart) and The William K. Warren Foundation

S91. Concordance Between Self-Report and Hair Analysis in the ABCD Study: Self-Report With Hair Analysis Detects Additional 10% of Substance Users

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Drug Category Other, Full panel drug toxicology
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The Adolescent Brain Cognitive Development (ABCD) Study is designed to investigate the impact of substance use onset in youth. To do this, the ABCD Study relies largely on self-report; however, it is unclear how accurate self-report of substance use is in adolescents. Use of more objective methods (i.e., hair toxicology) may reveal additional substance use. Here we aim to determine rates of substance use in both high risk and randomly selected low risk ABCD participants.
Methods: Data from the ABCD Study Annual Release 4.0 was used. Participants self-reported substance use on the Timeline Follow-back. Hair samples were collected from participants and tested using gas or

liquid chromatography with tandem mass spectrometry. A risk algorithm was used to select 1,287 high-risk youth samples for analysis; an additional 103 randomly selected low-risk samples were chosen for full toxicological analysis. Concordance between any self-reported substance use greater than puffing or sipping with hair toxicology was assessed using kappa coefficients.
Results: Between Baseline and Year 3, 5.5% of 1,390 ABCD youth self-reported substance use, while 10.4% were positive on accurate and reliable hair toxicology testing. In addition, when examining only randomly selected low risk participants, the confirmed positive rate was 6.7%. Concordance between self-report and hair results was significant but poor (kappa=0.05; p=.02). Use of hair results in addition to self-report identified an additional 9.4% of substance users, with a total of 14.9% of this sample identified as substance users.
Conclusions: The present findings suggest that use of both objective and self-report substance use metrics are important for accurately identifying adolescent substance use. This is true both in suspected users, but also in low-risk randomly selected participants. As most participants were carefully selected and the sample of randomly selected participants was small, more data is needed to better determine generalizability.
Financial Support: Supported by K08 DA050779 (PI: Wade) and F31DA054761 (PI: Sullivan).

S92. Considerations for Defining a Modified Completer Population in Human Abuse Potential Studies

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Drug Category Other, CNS drugs
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: Human abuse potential (HAP) studies have an enrichment design. Subjects selected for the Treatment Phase from the Qualification Phase should have a greater response to the positive control compared to placebo on the primary endpoint, Drug Liking (DL) Emax. However, some subjects respond to the positive control with a neutral DL Emax score, some have a negative difference in DL Emax scores between the positive control and placebo, and some have similar DL Emax scores to all treatments including placebo. These subjects may cause the study to be invalidated or produce inaccurate results. This study was performed to examine the prevalence of subjects who should not have been included in the Treatment Phase in past HAP studies and to develop criteria for a Modified Completer Population (MCP) to improve the assessment of HAP studies.
Methods: Fourteen HAP studies conducted after the publication of the 2017 FDA Guidance were examined. Elimination criteria for completers in the Treatment Phase were developed. The number of completers who met each elimination criterion in the Treatment Phase was obtained for each study. The percentage of subjects who met each elimination criterion in 14 studies was calculated. A subject who satisfied more than one elimination criterion was counted only once.
Results: Among 609 subjects in 14 studies, 8.4% of subjects had a neutral DL Emax score to the high dose of positive control; 1.6% of subjects had a negative difference in DL Emax scores between the high dose of the positive control and placebo; and 0.2% of subjects had similar DL Emax scores to all treatments in the study. Examples showed changes in results of treatment comparisons by eliminating subjects who were not qualified to be included in the assessment.
Conclusions: We recommend using elimination criteria to establish an MCP and using the MCP as the primary population in HAP studies.

S93. Prospective Effects of Financial Insecurity on Frequency of Substance Use

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Drug Category Other, General Substance Use
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Cross-sectional studies suggest that poverty and unemployment are associated with substance use, which may serve as a coping mechanism. However, few studies have used prospective data to examine

whether financial insecurity predicts subsequent substance use at the individual level. This study used prospective data from a community convenience sample of US adults to examine whether financial insecurity predicted subsequent increased substance use.
Methods: Participants were adults with problematic substance use (N=438), recruited between 05/2016–06/2019 from a New York City medical center. At baseline, 3-month, and 6-month follow-ups, participants completed identical computerized questionnaires. We used generalized estimating equations to assess the average effect of past 2-week financial insecurity on subsequent number of days of substance use, controlling for baseline days of use, demographic characteristics (i.e., sex, age, race/ethnicity, education, marital status, employment), and past 2-week DSM-5 depression.
Results: The sample was predominantly male (69.9%), non-Hispanic Black (59.1%), never married (58%), unemployed (78.3%), and had a high school education (57.3%). Compared with individuals who were able to meet their financial needs, participants who experienced financial insecurity in the past 2 weeks had a significantly higher frequency of substance use at the subsequent assessment (adjusted β=0.18 95% CI: 0.04-0.31). This relationship was strongest among those whose primary substance was opioids. Among individuals who used opioids, those experiencing financial insecurity had an average of 0.70 more days of substance use at the subsequent assessment compared with those able to meet financial needs (95% CI: 0.16-1.25).
Conclusions: Individuals experiencing financial insecurity reported more days of subsequent substance use than those able to meet their financial needs. This relationship was particularly pronounced among people who use opioids. This is cause for concern because US adults have experienced high rates of financial stress and insecurity due to pandemic-related stay-at-home orders.
Financial Support: This work was supported by grants T32DA031099 (Gutkind and Hasin [program director]), and R01DA018652 (Hasin) New York State Psychiatric Institute.

S94. Reinforcer Pathology's Anhedonia Hypothesis: An Examination Among Those in Recovery From Substance Use Disorder

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Drug Category Other, Recovery
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: Reinforcer Pathology theory provides a conceptual approach to understand the processes that result in excessive consumption of substances of abuse. The current study investigated the association between length of the temporal window (i.e., how far in the future one can imagine and integrate into present decisions; measured by delay discounting rates) and measures of anhedonia in individuals in recovery from substance use disorders. According to the anhedonia hypothesis of Reinforcer Pathology, individuals with shorter temporal windows will have higher levels of anhedonia, therefore, we hypothesize that length of the temporal window is inversely related to measures of anhedonia.
Methods: Data were collected from the International Quit and Recovery Registry from individuals in recovery from substance use disorders (N=223, 63.2% Male). Participants completed the 5-Trial Adjusting Delay Discounting Task, the Snaith-Hamilton Pleasure Scale and the Temporal Experiences of Pleasure Scale. Univariate linear regressions were performed to assess the association between the temporal window and measures of anhedonia. Multivariate regression with model selection was performed to determine the optimal model for measures of anhedonia.
Results: Delay discounting rate was significantly associated with levels of anhedonia, as measured by the Snaith-Hamilton Pleasure Scale ($p<0.001$) and the subscales of the Temporal Experiences of Pleasure Scale ($ps<0.001$). Furthermore, delay discounting ($ps<0.001$) persisted in the final model for each anhedonia measure after multivariate regression with model selection.
Conclusions: The current findings support the Reinforcer Pathology hypothesis that individuals in recovery from substance use with short temporal windows may have increased levels of anhedonia. Interventions, such as Episodic Future Thinking, to expand one's temporal window may improve treatment success and reduce the likelihood of relapse.
Financial Support: Fralin Biomedical Research Institute at Virginia Tech Carilion

S95. Cannabis Use and Mental Health Among Transition Age Youth Receiving Care in a Large Urban Healthcare System 2019-2020

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Transition Age Youth (TAY) are at high risk for problem cannabis use and its consequences. We describe the prevalence of cannabis use and diagnosed mental health conditions among TAY patients 18 – 29 years compared to older adults attending primary care (PC) in a large urban healthcare system.
Methods: We used EHR data July 2019–May 2020 from 60 PC clinics of patients' ≥ 18 years with annual physical examination. Current cannabis use was assessed by clinical staff. We also used EHR data on current mental health diagnoses (ICD-10) including depression, anxiety, sleep and opioid use disorders.
Results: 83,913 patients were included: 13.8% were TAY (18-29 years). Prevalence of cannabis use was highest among TAY: 22-25 years (27.4%), 26-29 years (24.8%), 18-21 years (21.4%), compared to 7.6% among age ≥ 50 years ($p<.01$). Prevalence of anxiety and depression was highest among TAY (10.3% and 8.6% respectively) and declined with age (4.5% and 4.6% respectively among age ≥ 50 years) ($p<.01$). Opioid use and sleep disorders were lowest among TAY (0.5% and 1.5% respectively) and increased with age (3.2% and 5.5% respectively among age ≥ 50 years). Cannabis use was significantly higher among TAY diagnosed with anxiety or depression and this differential was significantly more when compared to patients ≥ 50 years. For instance, among patients with depression vs. not having depression, prevalence of cannabis use was: 22-25-year-old (42.4% vs. 25.8%, $p<.01$), 50 years and older (11.2% vs. 7.4%, $p<.01$). In multivariable analyses, the interaction between age and cannabis use on the outcomes of depression and anxiety remained statistically significant.
Conclusions: The prevalence of cannabis use among TAY adults in PC is high and is higher among those diagnosed with anxiety or depression. TAY patients may benefit from routine PC screening for cannabis use and evaluation and treatment for associated mental health problems.
Financial Support: This work was supported by the University of California Tobacco-related Disease Research Program (TRDRP) grant number T29IR0277

S96. Shifting State-Level Cannabis Policies and Health Equity for Racial and Ethnic Minority Young People: A Qualitative Exploration

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Drug Category Cannabis/Cannabinoids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: Cannabis use is similar across racial/ethnic groups, yet Black or Hispanic people are four-times more likely than white people to be arrested for cannabis possession. Liberalizing cannabis policies could potentially address this disparity, especially in the 18 states with legal recreational cannabis or the 27 with decriminalization. We interviewed racial/ethnic minority youth and young adults (REMYYA) and community stakeholders to explore how liberalizing cannabis policies affects racial and health inequities for minoritized young people.
Methods: We interviewed 68 individuals from April 2018-January 2019. This included 30 REMYYA ages 18-29 years in New York City who identified as Hispanic and/or Black and 38 community stakeholders across states with various cannabis policies who worked at organizations focused on substance use and/or policies affecting youth. Interviews were recorded, transcribed and analyzed using thematic content analysis.

Results: Three main themes emerged about how cannabis policies directly and indirectly affect REMYYA health: 1) Benefits of Policy Liberalization. Policy liberalization allowed REMYYA to use cannabis: "for medical reasons, depression, bipolar, pains" and could increase access to needed services; stakeholders shared that homeless shelters often require negative cannabis screens, limiting REMYYA access. 2) Differential Policy Enforcement Alienates REMYYA. Policy liberalization increased REMYYA's sense of well-being because: "it takes a sense of panic off my back." However, police continue to weaponize cannabis enforcement to justify surveillance of specific neighborhoods, causing youth to feel othered in their own spaces; and 3) Legalization can Counter Racialized Criminalization. REMYYA called for legalization to limit arrests and related consequences that: "take them out of school, colleges, homework, and into jail."
Conclusions: REMYYA saw cannabis policy liberalization as a way to limit arrests and related consequences, increase personal security and service access, and reduce stress-related disorders. However, uneven policy implementation could exacerbate police-based racism and discrimination, and increase the consistent perceived and actual surveillance of REMYYA.
Financial Support: K01DA039804 (Philbin), K01DA045224 (Mauro)

S97. Trends in Cannabis Use Disorder Diagnoses in the U.S. Veterans Health Administration: 2005-2019

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: In the United States, adult cannabis use has increased over time, but information is lacking about U.S. time trends in Cannabis Use Disorder (CUD), including among veterans, or whether such trends differ by age (<35 years, 35-64 years, ≥65 years), sex or race/ethnicity.
Methods: Veterans Health Administration (VHA) electronic health records from 2005-2019 (n's: 4,403,027 to 5,797,240) were used to identify the percent of VHA patients seen in the U.S. each year with a CUD diagnosis (ICD-9-CM CUD, 1/1/2005-9/30/2015; ICD-10-CM CUD, 10/1/2015-12/31/2019). Trends in CUD diagnoses were examined by age, and by race/ethnicity and sex within age groups. Given the transition in ICD coding, differences in trends were tested within two periods: 2005-2014 (ICD-9-CM) and 2016-2019 (ICD-10-CM).
Results: In 2005, among patients age <35, 35-64 and ≥65, 1.70%, 1.59%, and 0.03% were diagnosed with CUD; by 2019, this had increased to 4.84%, 2.86% and 0.74%, respectively. Although men had consistently higher CUD prevalence than women, between 2016-2019, CUD increased more in female than male patients <35 years. Black patients had consistently higher CUD prevalence than other race/ethnic groups, and increases were greater in Black than White patients among those <35 years in both periods.
Conclusions: CUD diagnoses have increased substantially in VHA patients across age, sex and race/ethnic groups. Possible explanations warranting investigation include decreasing perception of cannabis risk, changing laws, increasing cannabis potency, stressors related to growing socioeconomic inequality, and use of cannabis to self-treat pain. Education about cannabis and CUD is needed for the public and for professionals, including VHA providers.
Financial Support: Support is acknowledged from the National Institute on Drug Abuse (R01DA048860) and from the Center of Excellence in Substance Addiction Treatment and Education, VA Puget Sound Health Care System.

MONDAY, JUNE 13, 2022

POSTER SESSION 2

M1. Augmenting a Low-Level Implementation Strategy to Address Co-Occurring Substance Use and Mental Health Disorders: Outcomes From the Adaptive Implementation of Effective Programs Trial (ADEPT)

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Drug Category Nicotine/Tobacco
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Evidence-Based Practices (EBPs) like Collaborative Care Models (CCMs) have the potential to improve the well-being of adults with co-occurring mental health and substance use disorders. Over 9.5 million individuals suffer from co-occurring disorders in the U.S. Tobacco use is a primary cause of morbidity and mortality among those with mental illnesses. In this study, we examined the impact of differing intensities of hands-on implementation support, facilitation, on cigarette use, and depression outcomes among sites unresponsive to a low-level implementation strategy to support uptake of the Life Goals CCM.
Methods: The study included community health clinics in 2 states that failed to achieve sufficient uptake of Life Goals after 6 months of low-level implementation support (Replicating Effective Programs:REP). We assessed cigarette use using Health Information National Trends Survey (HINTS) and depression using the PHQ-9. Sites (having <10 patients receiving LG or < 50% of patients receiving $\leq$3 Life Goals sessions) were randomized to REP with external and internal facilitation (EF/IF) or external facilitation (EF) only. EFs were outside experts supporting implementation and IFs were clinic staff with designated time to support Life Goals uptake.
Results: Seventeen clinics were randomized to either REP+EF or REP+EF/IF. Participant depression levels decreased over time, while cigarette use did not. We did not see differences in cigarette use by implementation strategy condition (EF versus EF/IF). We observed gender differences in depression, but no other demographics influenced depression or cigarette use.
Conclusions: Cigarette use outcomes may be attributed to low administration of Life Goals substance-use sessions (1.3%). Our results underscore the promise of integrated treatment approaches but suggest that additional strategy refinement is needed to achieve effective integration to address secondary outcomes including tobacco use. More work is needed to advance implementation strategies that facilitate integrated treatments for patients with co-occurring conditions as patients rarely receive treatment for both.
Financial Support: NIDA K01DA044279; NIMH R01 MH099898

M2. Open Board

M3. COVID Wariness, Protective Behaviors, Smoking, and Cigarette Purchasing Patterns Among Vulnerable Populations

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Drug Category Nicotine/Tobacco
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Populations vulnerable to smoking are disproportionately impacted by COVID-19. Little research has focused on whether people who smoke have adopted COVID-related protective behaviors (e.g., mask wearing). Though overall cigarette sales increased during the pandemic, some smokers modified their cigarette purchasing patterns to reduce infection risk. We examined associations between COVID wariness and adoption of COVID-related protective behaviors, changes in smoking, and changes in cigarette purchasing patterns among vulnerable smokers.
Methods: Web-based surveys were distributed to 709 adults who had participated in a previous trial investigating the effects of very low nicotine content cigarettes in daily smokers with socioeconomic disadvantage, comorbid affective disorders or opioid use disorder. COVID wariness was rated on three scales: perceived probability of being infected by COVID (probability), likely disease severity upon infection (severity), and perceived personal susceptibility to COVID (susceptibility). Associations between COVID wariness scales and self-reported adoption of COVID-related protective behaviors, changes in

smoking, and changes in cigarette purchasing patterns were examined using Chi-square and Fisher's Exact tests.
Results: Among respondents (N=440, 55.2% female), adoption of protective health behaviors was high (all behaviors endorsed by >85% of respondents). COVID wariness was positively associated with perception of smoking as a risk factor for COVID (p's≤.01). Greater severity was associated with avoiding touching one's face, using hand sanitizer, and staying home except for essential reasons (p's<.05). Greater susceptibility was associated with avoiding touching one's face while smoking (p=.03). Smoking rate and cigarette purchasing patterns were generally unrelated to COVID wariness scales, though there was a association between greater severity and buying more packs of cigarettes per store visit (p=.03).
Conclusions: Among vulnerable smokers, COVID wariness was associated with adoption of protective behaviors but was generally unrelated to changes in smoking or cigarette purchasing behavior. Vulnerable smokers may be unable to reduce smoking even during public health crises.
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M4. Flavor Compounds Modulate Oral Nicotine Consumption and Preference in Mice

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The use of electronic cigarettes (e-cigarettes) has been steadily increasing over the last 15 years. E-cigarettes are available in a wide range of flavors that increase their attractiveness and use. However, the impact of individual flavor compounds on nicotine consumption and preference is not well understood. The objective of this study was to compare the effect of flavor compounds found either in fruit-flavored e-cigarettes (trans-2-hexanol) or tobacco-flavored e-cigarettes (beta-damascone) in a mouse model of nicotine consumption. We hypothesized that trans-2-hexenal (T2H) would increase nicotine consumption and preference, whereas beta-damascone (BD) would have no effect on nicotine consumption and preference.
Methods: Adult male mice (n=14-15) voluntarily consumed 75ug/mL nicotine alone, nicotine with a flavor compound or a flavor compound alone in a series of voluntary, chronic two-bottle choice tests. The concentration of flavor compound was increased weekly over five weeks (0.1, 1, 10, 50, 100 ug/mL) while the nicotine concentration remained at 75 ug/mL. We measured the average nicotine consumption (mg/kg/day) and percent preference for the nicotine or flavor bottle, and data was analyzed using repeated measures 2-way ANOVA with multiple comparisons tests.
Results: We found that T2H alone at the lowest concentration tested of 0.1 ug/mL resulted in higher consumption than nicotine alone (P=0.01) and trended towards higher preference compared with nicotine alone (P=0.05). The addition of BD significantly decreased nicotine consumption and preference at the 1 and 10 ug/mL concentrations (P<0.0001 and P<0.0001, respectively).
Conclusions: These data indicate that flavor compounds can differentially modulate voluntary nicotine consumption and preference, which can have important implications for the inclusion of flavor compounds in e-cigarette formulations.
Financial Support: NIH R01 AA026598 (A.M.L.)

M5. Interactive Effects of Financial Strain and Distress Tolerance on Pre-Quit Tobacco Withdrawal Symptoms in Smokers Preparing to Initiate a Quit Attempt

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Drug Category Nicotine/Tobacco
Topic Disparities

Abstract Detail Human
Abstract Category Original Research
Aim: Smokers experiencing greater financial strain are less likely to successfully quit smoking, possibly due to greater severity of tobacco withdrawal symptoms. However, scarce work has explored whether specific psychological traits, such as distress tolerance, may buffer the deleterious effects of financial strain on tobacco withdrawal. The current study examined the main and interactive effects of financial strain and distress tolerance on tobacco withdrawal prior to quitting smoking amongst smokers preparing to initiate a quit attempt.
Methods: 116 daily cigarette smokers (35.3% Female; M age=33.14 years old) interested in quitting smoking completed a baseline session including a self-report measure of financial strain and subjective and behavioral assessments of distress tolerance. Participants were then instructed to initiate a quit attempt without any assistance within 14 days following the baseline session. Daily experiences of tobacco withdrawal symptoms were assessed for a period of three days prior to the scheduled quit date via daily diaries. Linear regression models were conducted to evaluate main and interactive effects between financial strain and distress tolerance assessments on severity of daily withdrawal symptoms prior to quitting.
Results: Findings demonstrated significant interactions between financial strain, distress tolerance, and tobacco withdrawal. Among smokers reporting high financial strain, those with lower (vs. higher) levels of distress tolerance reported greater perceptions of tobacco withdrawal and negative mood-related symptoms as being more “difficult to tolerate" prior to quitting (Beta interaction terms=-.36 to -.28, ps<.005).
Conclusions: Financial strain may negatively impact one’s perceived ability to tolerate mood- and tobacco-related withdrawal prior to a quit attempt, yet higher distress tolerance may serve as a protective factor to mitigate the effects of financial strain on smoking cessation processes. Psychosocial interventions designed to promote tolerance of distress originating from internal and external sources, such as financial strain, may benefit smoking cessation efforts among socioeconomically disadvantaged smokers.
Financial Support: This research was supported by National Institute on Drug Abuse of the National Institutes of Health Grants F31DA026634 and K23DA046482 (PI: Kirsten Langdon), K24DA048160-03 (PI: Adam Leventhal), and National Science Foundation Graduate Research Fellowship Grant DGE-1418060 (PI: Mariel Bello).

M6. Pattern of Tobacco Use and Nicotine Dependence in Patients With Psychiatric Disorders

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Drug Category Nicotine/Tobacco
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of the current study was to assess prevalence of nicotine dependence in male patients with other psychiatric disorders.
Methods: A cross-sectional study was conducted in Psychiatry department of a tertiary health care facility in north India. Male Patients having any psychiatric disorder as per ICD 10 along with Nicotine use disorder were enrolled for the study. Socio-demographics, clinical details and psychiatric disorder details including nicotine use were collected.
Results: The most common psychiatric disorder reported were- schizophrenia (n=28, 32.2%), anxiety (n=23, 26.4%) and bipolar disorder (n=22, 25.3%). The mean age of patients with schizophrenia, anxiety, bipolar disorder and depression were 31.8 (9.7), 42.2 (10.7), 37.6 (13.1) and 36.5 (11.6) respectively. The mean age of onset of schizophrenia, anxiety, bipolar disorder and depression were 21.6 (4.7), 33.1 (12.3), 27.4 (8.6) and 30.1 (11.7). Smoking was the most common form of nicotine use in all the psychiatric disorders. The mean FTND and FTND-ST score were 2.3 (1.4) and 0.64 (.9) respectively. No correlation was observed between age of onset of psychiatric disorders and smoking severity.
Conclusions: Patient with different psychiatric disorders do not necessarily have high level of nicotine dependence.

M7. Youth Susceptibility to Tobacco-Free Oral Nicotine Products in Comparison to Cigarettes and E-Cigarettes

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To examine susceptibility to inhalable and oral nicotine product use in a youth cohort.
Methods: Ninth- and tenth-grade students from Southern California completed an online survey in Fall 2021 assessing susceptibility to inhalable (i.e., cigarettes, e-cigarettes) and oral (e.g., pouches, gum, gummies) nicotine products among youth with no history of any nicotine product use. Multinomial logistic regression analyses evaluated whether likelihood of susceptibility to inhalable products, oral products, or both products differed across sociodemographic groups.
Results: The analytic sample (N=3,130) was 46.5% female and 44.9% Hispanic. Most participants (73.3%) were not susceptible to inhalable or oral nicotine product use; 12.7% were susceptible to both, 11.1% to inhalable products only, and 2.9% to oral products only. Compared to males, females (inhalable: OR=1.62; 95%CI: [1.27,2.07]; both: OR=1.55[1.24,1.95]) and youth of other genders (inhalable: OR=2.73[1.85,4.04]; both: OR=2.31[1.57,3.39]) were more likely to be susceptible to inhalable products and to both oral and inhalable products. Compared to Asian youth, Hispanic youth were more likely to be susceptible to inhalable only (OR=1.51[1.16,1.97]) and to both products (OR=1.55[1.21,1.98]). Lower-socioeconomic status (SES) youth (inhalable: OR=1.75[1.33,2.31]; both: OR=1.53[1.17,2.01]; oral: OR=1.96[1.20,3.18]) and sexual minority youth (inhalable: OR=2.08[1.61,2.69]; both: OR=2.35[1.85,2.98]; oral: OR=2.25[1.43,3.53]) were more likely to be susceptible to oral products, inhalable products, and both products, compared to higher-SES and heterosexual youth.
Conclusions: Youth nicotine never-users reported susceptibility to oral nicotine product use, with disparities evident by SES and sexual identity. Oral nicotine products may attract some youth who would not otherwise use nicotine, including youth from vulnerable populations.
Financial Support: National Cancer Institute and FDA Center for Tobacco Products U54CA180905;
National Cancer Institute R01CA229617;
National Institute on Drug Abuse K24DA048160;
National Heart, Lung and Blood Institute K01HL148907

M8. Association Between Electronic Cigarette and Combustible Cigarette Use With Cardiometabolic Risk Biomarkers Among U.S. Adults

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The objectives were to determine the association of cigarette behaviors (i.e., non-users, exclusive e-cigarette users, exclusive combustible cigarette users, and dual users of both products) with cardiometabolic risk biomarkers.
Methods: Data came from the National Health and Nutrition Examination Survey (NHANES), a nationally representative survey of the US population, across two cycles conducted between 2015-2016 and 2017-2018. Of the 19.225 participants, we excluded those < 18 years of age (n=7,377), those with a history of cardiovascular disease or diabetes (n=2,553) or who have missing information on these medical conditions (n=598) and those with missing data on cigarette use behaviors (n=9). We determined the association of cigarette use behaviors and reduced high-density lipoprotein cholesterol (HDL-C; <40 mg/dL, for men and <50 mg/dL for women), elevated low-density lipoprotein cholesterol (LDL-C; ≥130 mg/dL), elevated triglycerides (TG; ≥150 mg/dL), elevated fasting blood glucose (FBG; (≥100 mg/dL), and high blood pressure (HBP; Systolic ≥130 mm Hg/Diastolic ≥85 mm Hg).
Results: Of the 8,688 participants included, 2.8%, 3.2% and 14.5% self-reported exclusive e-cigarette, dual product use, and exclusive smoking respectively. After adjusting for covariates and further excluding former smokers (n=1,715), exclusive e-cigarette use (compared to non-users) was statistically significantly

associated with increased odds of HBP (adjusted odds ratio (aOR)=2.05, 95% confidence interval (CI)=1.03, 4.08), no other associations were statistically significant. Dual use (compared to non-users) was associated with increased odds of HDL-C (aOR= 1.64, 95% (CI): =1.01, 2.70). Exclusive combustible cigarette smoking (compared to non-users) was statistically significantly associated with reduced HDL-C (aOR=1.80, 95% (CI)=1.45, 2.23) and elevated TG (aOR=1.59, 95% (CI)=1.01, 2.52).
Conclusions: Participants who self-reported exclusive e-cigarette use, had higher odds of HBP, whereas we found no statistically significant difference in abnormal serum lipid levels. Additional studies using larger samples of exclusive e-cigarette users, that capture frequency and duration of use with longitudinal follow-up is warranted.
Financial Support: K01DA047912

M9. Changes in Smoking From 2018 to 2020 Among Older Adults in the US: Implications for COVID-19

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Cigarette smoking could directly increase COVID-19 risk. However, little is known about changes in smoking patterns before and during the ongoing pandemic among older adults, who have been most severely affected by COVID-19 mortality.
Methods: Data were obtained from 3,095 adults ages 50 and older in the preliminary Health and Retirement Study (HRS) COVID-19 Project, collected starting in June 2020 (data released in November 2020) and merged with 2018 HRS data. We used self-reported smoking status (never, former, current) and number of cigarettes per day to categorize smoking intensity changes from 2018 to 2020: increase/re-initiation, decrease/cessation, and no change (which differentiated people with a history of smoking [former/current] from those who never smoked). Survey-weighted multinomial logistic regressions estimated associations between smoking intensity change and socio-demographic characteristics.
Results: In late 2020, 11.86% of participants reported currently smoking and 38.62% formerly smoked. While almost all participants maintained their smoking status between years, 1.24% re-initiated and 1.89% ceased smoking. Based on average number of cigarettes smoked, 4.33% reduced while 9.96% increased smoking intensity. Compared to the 41.76% of people with a smoking history reporting no change in smoking intensity from 2018 to 2020, increases in smoking intensity were less likely among people 65+ vs. 50-64 (aRRR=0.28, 95% CI=0.17, 0.48) and more likely among people in the Midwest vs. Northeast (aRRR=2.84, 95% CI=1.29, 6.24). Average smoking intensity remained constant among people reporting currently smoking in both 2018 and 2020 (mean=-0.50; 95% CI=-1.60, 0.59).
Conclusions: One in ten older adults increased their smoking behaviors from 2018 to 2020. Sociodemographic and geographic differences were consistent with subgroups disproportionately affected during the first wave of the COVID-19 pandemic. Improved cessation support services are needed to mitigate risk as the pandemic continues to evolve, especially among older adults who continue to smoke or have increased smoking intensity.
Financial Support: K01DA045224 (PI: Mauro), T32DA031099 (Gutkind, PI: Hasin), DP5OD023064 (PI: Giovenco)

M10. Characterization of Nicotine Pharmacokinetics and Pharmacodynamics During Use of Five Commercially Available Nicotine Pouches and Two Nicotine Lozenges in Adult Cigarette Smokers

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research

Aim: Oral tobacco-derived nicotine products are a rapidly emerging tobacco category that may offer noncombustible alternatives to adult smokers (AS) unable or unwilling to quit. In this study we characterized nicotine pharmacokinetics (Nic-PK) and pharmacodynamics of five commercially available nicotine pouches (labeled nicotine: 4mg, "medium," 6mg, 7mg, 8mg) and two nicotine lozenges (labeled: 2mg and 4mg).
Methods: AS (n=34, 21 male) participated in a randomized crossover study that measured Nic PK and PD measurements including heart rate (HR; beats per minute [bpm]) over 120mins during a 30-min product use period, subjective measures about urges to smoke, craving cigarettes, and how "pleasant" products were rated.
Results: Nicotine Cmax (Geometric Least Square Mean (GLSMean), ng/ml) was 3.0(4mg pouch), 5.6(medium), 11.4(6mg), 8.9(7mg), 15.0(8mg), 3.1(2mg lozenge), and 4.1(4mg lozenge). The median tmax was slower than historical cigarette data (i.e., <10min) and ranged from 30-35min (pouches), 36min(2mg lozenges), and 90min(4mg lozenges). The GLSMean HR increase ranged from 8.9-13.9bpm(pouches) and corresponded with the Cmax. Lozenges increased HR by 8.4bpm(2mg) and 9.9bpm(4mg). All products reduced ratings of urge to smoke and craving cigarettes; reductions generally followed Cmax, but were lower than reported cigarette values. All products increased ratings of "pleasant," but with no clear relationship to Cmax. While nicotine delivery generally followed the labeled amount, product design can influence nicotine delivery, as illustrated by the 6mg and 7mg pouches and the tmax for the lozenges.
Conclusions: Overall, the oral nicotine products delivered a range of nicotine levels and reduced the urge to smoke/craving a cigarette, suggesting that they may serve as switching products for AS. The PD measurements were not as discernable as the Nic-PK for the different products. The Nic-PK profiles suggests that nicotine might be absorbed through the buccal mucosa for the pouches and through the buccal mucosa and the gastrointestinal tract for the lozenges.

M11. Pulsed Intravenous Nicotine Infusions as Model for Inhaled Tobacco Use in Humans

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: The dose and speed at which drugs are delivered to brain can influence their abuse liability. We have used a precise intravenous (IV) administration paradigm to administer nicotine in various doses and IV pulsed-infusions – thereby modeling the puffing of cigarettes and e-cigarettes in humans. The specific aim of this study was to examine the impact of dose and delivery rate on subjective drug effects, urges to smoke, nicotine withdrawal, and heart rate.
Methods: Following overnight abstinence from smoking, a total of 11 (45% female, 28.5 ± 3.5 years old) dependent smokers attended 5 experimental sessions. In each session, using a crossover design, participants were assigned to 1 of 5 conditions involving nicotine- or saline-pulsed infusions ("pulses"): 1) High Dose/Fast Delivery: 1.0 mg/70kg nicotine delivered over 5 pulses; 2) High Dose/Slow Delivery: 1.0 mg nicotine delivered over 20 pulses; 3) Low Dose/Fast Delivery: 0.2 mg/70 kg nicotine delivered over 5 pulses; 4) Low Dose /Slow Delivery 0.2 mg/70 kg nicotine delivered over 20 pulses; and 5) Placebo, delivered over 20 pulses. Subjective drug effects, urges to smoke, nicotine withdrawal and heart rate were analyzed using mixed models with dose, time, and dose by time interaction as fixed effects.
Results: Both the High/Fast and High/Slow conditions were associated with greater "Head Rush" ($F(4,235)=2.86$, $p<0.05$), indexed by the Drug Effects Questionnaire. The High/Fast condition also provided greater suppression of urges to smoke ($F(4,235)=3.05$, $p=0.02$), and nicotine withdrawal ($F(4,225)=4.38$, $p=0.002$), indexed by the Questionnaire of Urges to Smoke-Brief, and the Minnesota Nicotine Withdrawal Scale, respectively. Finally, the High/Fast and High/Slow produced greater increases in heart rate ($F(4,35)=5.45$, $p=0.002$) than the other conditions.
Conclusions: These preliminary findings support the ecological validity of our innovative human laboratory model, which can be used to study novel smoking cessation therapies and nicotine reduction approaches for tobacco regulation.
Financial Support: VA VISN-1 Mental Illness Research, Education, and Clinical Center

M12. The Relationship Between Nonsystematic Delay Discounting and Low-Quality Survey Responses in a Sample of Smokers: ROC Curve Analysis

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Drug Category Nicotine/Tobacco
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: Delay discounting (DD), the decrease of the subjective value of a reward with the increase of the delay to its receipt, is associated with various substance use disorders. As evidence continues to mount regarding DD's status as a transdiagnostic process, additional attention needs to be given to nonsystematic DD, a response pattern that has been reported in the literature but rarely investigated. In our recent online research, we noticed an increase in the proportion of nonsystematic DD responses across samples, consistent with the so-called Amazon Mechanical Turk data quality crisis. The significant proportion of nonsystematic responses created the opportunity for investigation in the current study, in which we hypothesized that nonsystematic DD was associated with low-quality survey responses.
Methods: A sample of smokers of both sexes recruited from Mturk (n = 210) completed a DD task and questionnaires about tobacco use and demographics. Participants' response quality was evaluated by three independent quality check indexes created for the study. The degree of nonsystematic DD was quantified by the algorithms developed by Johnson and Bickel (2008). The area under the curve (AUC) of the receiver operating characteristic (ROC) curve predicting response quality by nonsystematic DD was obtained. The observed AUC was pitted against a simulated distribution reflecting the null hypothesis that the observed association was due to chance in a permutation test.
Results: The observed AUC values were at the extreme of the null distributions (ps < .001). Furthermore, the nonsystematic DD cutoffs provided in Johnson and Bickel (2008) showed good sensitivity (0.77-0.93), albeit poor specificity (0.42-0.74), in detecting low-quality responses.
Conclusions: Nonsystematic DD was associated with low-quality responses, although other factors contributing to the nonsystematic responses remained to be identified. Our findings provide support to exclude nonsystematic DD data from analysis in the field of addiction.
Financial Support: This work was supported by the Fralin Biomedical Research Institute at Virginia Tech Carilion.

M13. Tobacco, Alcohol, Cannabis, and Other Drug Use in the U.S. Before (2016-2019) and During (2020) the COVID-19 Pandemic: Findings From the Path Study

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: During 2020, tobacco, alcohol, cannabis, and other drug use in the U.S. may have been affected by coinciding factors, including the COVID-19 pandemic, and changing tobacco and cannabis policies. Therefore, we examined the prevalence of substance use among youth and adults before and during 2020.
Methods: We used nationally representative data from youth (13-17-year-olds, N=17,581) and adults (≥18 years, N=40,406) enrolled in the Wave (W) 4 cohort of the Population Assessment of Tobacco and Health Study and interviewed at least once between 2016 and 2020. Data were collected in-person at W4 (December 2016-January 2018), W4.5 (December 2017-December 2018; youth only), and W5 (December 2018-November 2019) and via telephone in W5.5 (July-December 2020; youth only) and the Adult Telephone Survey (September-December 2020). At each wave, we estimated the age-stratified prevalence and 95% confidence intervals (CI) of self-reported past-30-day use of any tobacco (including e-products), alcohol and binge drinking, cannabis, and other illegal or misused prescription drugs.
Results: Among youth, there were minor changes in use from 2016-2019. All substance use decreased significantly from 2019 to 2020, with the greatest decline in past 30-day any tobacco use (13-15-year-olds:

6.9% [95% CI: 6.3, 7.7] in 2019 to 2.6% [95% CI: 2.1, 3.3] in 2020; 16-17-year-olds: 19.5% [95% CI: 18.4, 20.7] in 2019 to 9.2% [95% CI: 8.2, 10.4] in 2020). From 2019 to 2020, among 18-20-year-olds, there were significant decreases in all substances other than alcohol while in adults ≥21 years, we saw slight but significant decreases in any tobacco use.
Conclusions: Self-reported past-30-day substance use among youth was substantially lower in 2020 than in previous years. These results should be interpreted with caution given the change in mode and timing of data collection during the pandemic. Further investigation can determine contributing factors, such as effects of the pandemic or policy changes.
Financial Support: This research is supported with Federal funds from the National Institute on Drug Abuse, National Institutes of Health, and the Center for Tobacco Products, Food and Drug Administration, Department of Health and Human Services, under contract to Westat (Contract No. HHSN271201600001C).

M14. White Matter Integrity Among Early Nicotine Exposure in Early-Adolescence: An Adolescent Brain Cognitive Development (ABCD) Study

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Drug Category Nicotine/Tobacco
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: Nicotine usage has been steadily increasing among adolescents. A popular method of nicotine administration is electronic nicotine delivery systems (ENDS), such as e-cigarettes. Studies on white matter (WM) changes measured by diffusion tensor imaging (DTI) have associated adolescent nicotine usage with increased fractional anisotropy (FA), but primarily examined older adolescents using combustible tobacco products. Research of ENDS on WM is understudied; thus, here we examine differences in early nicotine exposure and WM integrity in adolescents, who primarily use ENDS.
Methods: Forty adolescents (10-13) with nicotine exposure were examined against randomly selected demographically-matched controls (n=80; 46 male) from the ABCD Study (4.0 release, 2-year follow-up). Of the 40 nicotine-using youth, 27 used only ENDS and a matched control set was selected for ENDS-use only analyses (n=54; 26 male). Participants underwent a DTI MRI scan and a drug use interview. FA and MD for tracts of interest were derived using Freesurfer. Linear models examined impact of low nicotine exposure on WM integrity while controlling for age, sex, race, ethnicity, and parental education.
Results: Models indicated significantly increased FA in the right inferior longitudinal fasciculus (rILF) and decreased MD in the right superior longitudinal fasciculus (rSLF) for youth with low-level nicotine exposure compared to controls. For ENDs-only analyses, no significant differences were found.
Conclusions: The current study found low-level nicotine usage during early adolescence is associated with greater FA in rILF and lower MD in rSLF. This is consistent with previous findings that adolescent nicotine exposure was linked with increases in FA and decreases in MD. ILF demonstrates early and fast maturation, thus nicotine initiation may affect this developmental trajectory early on. Conversely, ILF development may place youth at increased risk for nicotine use initiation. Future analyses should examine escalating nicotine use links between changes in WM development during adolescence.
Financial Support: U01DAO41025; PI: Lisdahl, K.M.; F31DA054761, PI: Sullivan, R.M.

M15. Open Board

M16. Characterizing Prevalence of Tobacco Product Type and Effects on Abstinence Among Individuals With Serious Mental Illness Enrolled in a Pragmatic Randomized Trial

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Drug Category Nicotine/Tobacco
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Consumption of non-cigarette tobacco products (e.g., little cigars [LCs]) is on the rise in the US. Individuals with serious mental illness (SMI) have increased rates of tobacco use. However, little work has investigated prevalence of different tobacco product types (TPT) or impact of TPT on cessation among those with SMI. We investigated prevalence and correlates of TPT, and impact of TPT on verified tobacco abstinence at follow-up among individuals with SMI enrolled in a large pragmatic tobacco cessation trial.
Methods: Secondary analysis of a single-cohort (N=1010) of a cluster RCT with outpatient community clinics assigned to academic detailing (AD) or usual care, with participant-level randomization within the AD arm to community health worker support (CHW+AD) vs. AD alone. Participants were surveyed at baseline on demographic and smoking characteristics including TPT use (cigarettes, LCs, roll-your-own cigarettes, e-cigarettes; select all that apply), and breath CO was collected. A TPT variable was derived for analyses (cigarettes/rollies; LCs; dual use). The primary outcome was biochemically-verified tobacco abstinence at Year 2.
Results: At baseline, 83% of participants reported using cigarettes, 33% LCs, 7% roll-your-own-cigarettes, and 1% e-cigarettes. 25% reported use of >1 product. Compared to cigarette/rollie or LC users, dual users of both products were more likely to be Black vs. other races and live in group vs. independent housing (p's<.05). LC users were older, used more tobacco products/day, and had higher COs vs. cigarette/rollie or dual users (p's<.05). At Year 2, 11%, 10%, and 4% of cigarette/rollie, LC, and dual users were verified abstinent, respectively (p=0.06), with higher abstinence rates observed among those randomized to receive CHW support. In adjusted logistic regression, TPT was not associated with Year 2 abstinence.
Conclusions: Individuals with SMI who use LCs have increased nicotine intake compared to other TPTs and lower rates of confirmed tobacco abstinence.
Financial Support: This work was funded by the Patient Centered Outcomes Research Institute (PCORI) Large Pragmatic Trial, 1504-30472; Integrated Smoking Cessation Treatment for Smokers with Serious Mental Illnesses; PI: A.E. Evins. Support for JMS and KS was provided by NIDA K12 DA043490 (PI: A.E. Evins).

M17. Discrepancies in the Relation Between Smoking and Performance Across Different Tests of Executive Function

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Drug Category Nicotine/Tobacco
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Smokers often exhibit impairments in executive function (EF), a broad category of higher-level thinking processes. The present study examined the generality of these impairments across different EF measures and their relation with smoking levels in vulnerable populations. Our hypothesis is that higher smoking levels are associated with greater EF impairment.
Methods: We used intake data from a prior study examining responses to reduced-nicotine-content cigarettes in 775 (28.9% male) adult verified smokers (breath carbon monoxide (CO) >8 ppm) selected from three populations highly vulnerable to smoking (low socio economic status women of reproductive age, opioid-maintained individuals, and individuals with affective disorders). Smoking measures included assessments of volume – cigarettes/day (CPD), CO, and blood-cotinine levels – and nicotine dependence – Fagerstrom Test for Nicotine Dependence (FTND) and heaviness of smoking index (HSI) scores. EF was assessed with stop-signal reaction times (SSRTs, response inhibition), n-back scores (n = 0 and 2, working memory), and nicotine Stroop task scores (nicotine-induced cognitive interference). Associations were examined using linear regressions while controlling for population, sex, menthol status, age, and education.
Results: Consistent with our hypothesis, FTND ($F(1,705)=6.17$, $p=0.01$), and HSI scores ($F(1,705)=4.13$, $p=0.04$) were positively associated with greater SSRTs (impaired inhibition). Similarly, FTND scores ($F(1,670)=6.55$, $p=0.01$) were negatively associated with 2-back accuracy (impaired working memory). No other significant associations were noted.
Conclusions: Smoking-related impairments in response inhibition and working memory were noted, but those in inhibition of cognitive interference were not. Among smoking measures only those for nicotine-dependence were significant, with greater dependence associated with greater EF impairment. These results

illustrate that while smoking is associated with EF impairments, more remains to be learned about their breadth and specificity.
Financial Support: Tobacco Centers of Regulatory Science (TCORS) Award U54DA036114 from the National Institute on Drug Abuse (NIDA) and Food and Drug Administration (FDA), and Centers of Biomedical Research Excellence Award P20GM103644 from the National Institute of General Medical Sciences (NIGMS). Content is solely the authors' responsibility and does not necessarily represent the official views of these institutions.

M18. Does Risky Substance Use Modify the Relationship Between Intensity of Nicotine Dependence and Motivation to Stop Smoking During COVID-19?

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Drug Category Nicotine/Tobacco
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: To investigate if risky substance use modifies the relationship between intensity of nicotine dependence and motivation to stop smoking among adults interested in reducing or quitting tobacco smoking.
Methods: Baseline electronic survey data from a micro-randomized text messaging ecological momentary intervention to reduce tobacco smoking were collected via Facebook recruitment from June to December 2021. Fagerstrom Test for Nicotine Dependence (FND) measured intensity of nicotine dependence, three motivation rulers for smoking cessation (Boudreaux et al., 2012) measured motivation to stop smoking, and the Alcohol Use Disorders Identification Test (AUDIT) and Drug Abuse Screening Test (DAST) measured risky substance use. We conducted stratified multiple logistic regression modeling with adjustment for demographic covariates.
Results: Of 80 participants, 52.2% (n=42) reported stopping smoking as a highly important goal in their life. 56.3% (n=45) reported readiness and 43.8% (n=35) confidence in quitting smoking within the next month. 36.3% (n=29) reported current other risky substance use. There was no significant association between intensity of nicotine dependence and readiness or confidence to quit smoking, regardless of other risky substance use. Other risky substance use modified the relationship between intensity of nicotine dependence and importance of stopping smoking (OR=0.52, 95% CI=0.30, 0.92). Among participants without other risky substance use, a one unit increase in the FND score was associated with 48.9% increase in the odds of reporting stopping smoking as a highly important life goal. There was no similar relationship among participants with risky substance use.
Conclusions: Among adults interested in reducing or quitting smoking tobacco, risky substance use may modify the relationship between intensity of nicotine dependence and the importance of stopping smoking. Within our sample, intensity of nicotine dependence has no meaningful relationship with readiness or confidence to quit smoking regardless of other risky substance use at baseline.
Financial Support: Supported by NIH/NIDA P30DA029926 and T32DA037202.

M19. Loss Aversion, Substance-Free Reward, and Risk for Cigarette Smoking and Other Substance Use

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Drug Category Nicotine/Tobacco
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: We recently identified an association between individual differences in loss aversion, a bias in decision-making wherein losses are valued greater than gains, and cigarette smoking and other addiction risk. The study aimed to replicate and extend the analysis to examine the possible moderating influence of substance-free rewards.
Methods: We recruited current daily cigarette smokers (n = 186; > 10 cigarettes per day) and never-smokers (n = 241; < 100 cigarettes lifetime) from the United States using Amazon Mechanical Turk. Groups were

matched on gender, educational attainment, and age. All completed items related to current cigarette smoking, alcohol use, other drug use, sleep problems, and depressed mood, task-based measures of loss aversion and delay discounting, a decision-making bias associated with cigarette smoking, and the reward probability index (RPI).
Results: Smokers were less loss averse than never-smokers even after accounting for delay discounting. Loss aversion was also a significant independent risk factor for alcohol and other drug use, although not other behavioral-health conditions (i.e., sleep disturbance, depressed mood). Smokers scored lower on the RPI than never smokers. Analyses of RPI subscales revealed that smoking was associated with significantly greater environmental suppression of reward, but smokers and never-smokers did not differ in measured ability to obtain reinforcement.
Conclusions: In addition to replicating the association between low loss aversion and current cigarette smoking and other substance use patterns, loss aversion was also strongly related to level of environmental barriers to nondrug reward. Loss aversion may warrant attention as a protective factor and potential target for preventive intervention for substance use and addiction.
Financial Support: NIH Grants: K01-DA044456, U54-DA036114, P20-GM103644

M20. Pilot Study Investigating Rapid Visual Information Processing Task Assessment of Nicotine Delivery Via Oral Nicotine Pouch Products

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: Lower-risk, non-combustible alternatives to cigarettes need to deliver sufficient nicotine in a manner to facilitate adult smokers (AS) switching. A challenge to developing potentially reduced harm tobacco products is the lack of objective, non-invasive, rapid measures of nicotine delivery. This pilot study explored whether cognitive task performance is sensitive to varying levels of nicotine via on!® nicotine pouches (NP) versus a nicotine-free oral pouch product.
Methods: We used a single-blind, randomized, crossover design to examine change in cognitive performance following use of flavor-matched oral pouches with and without nicotine (0, 2, 4, 8mg). Twenty-one AS not interested in quitting smoking and with no prior NP experience completed 6 sessions: screening/consent, task familiarization/training, and four experimental sessions following overnight abstinence, varying only in nicotine level. Abstinence was verified via expired CO (≤10ppm). Cognitive assessment was investigated via Rapid Visual Information Processing (RVIP) at baseline and immediately after using the assigned product for 15 minutes. During each 7-minute RVIP, participants saw a series of single-digit numbers and responded when pre-specified 3-digit target sequences appeared (e.g., 3-5-7). Outcomes included target detection/sensitivity and Median Reaction Time (MRT) for correct responses.
Results: There was a statistically significant effect of nicotine level on mean change from baseline (CFB) for target detection, $p<0.05$. Follow-ups comparing NPs vs nicotine-free pouches revealed statistically significant greater CFB (improved performance) for 8mg ($p<0.01$), but not 4mg and 2mg—however, similar trends were observed. There was no significant effect of nicotine level on MRT CFB.
Conclusions: Sustained attention (target detection), but not reaction time, was sensitive to differences between nicotine- and non-nicotine oral pouches used after overnight abstinence only discernable at the highest nicotine level tested, 8mg. Further studies may be needed to establish the utility of this method as a non-invasive tool in development of potentially reduced harm tobacco products.
Financial Support: This work was funded by Altria Client Services LLC and all authors are/were employees of Altria Client Services LLC.

M21. Sexual Identity Differences in Perceived Risk of Tobacco and Marijuana Use Among U.S. Young Adults

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Young adults who identify as gay, lesbian, or bisexual (LGB) are more likely than heterosexual-identifying peers to use tobacco and marijuana. Sexual identity differences in susceptibility to tobacco and marijuana use initiation are less well understood. Prior research demonstrates that individuals who perceive substance use as risky are less likely to initiate use. This study examined sexual identity differences in tobacco and marijuana risk perceptions among never-using individuals.
Methods: Data were from the 2015-2019 National Survey on Drug Use and Health. Our sample was restricted to individuals ages 18-34 year old who identified as heterosexual, lesbian/gay, or bisexual. Using weighted logistic regression stratified by sex, we examined sexual identity differences in the perceived level of risk (great risk vs. not) of (1) smoking 1+ packs of cigarettes per day among men and women who reported never smoking cigarettes (n=49,429) and (2) using marijuana once per month or using marijuana 1-2 times per week among men and women who reported never using marijuana (n=50,511).
Results: AAmong those who had never smoked cigarettes, bisexual men (aOR=0.77[95%CI=0.62,0.97]) and bisexual women (aOR=0.78[95%CI=0.68,0.89]) were significantly less likely to perceive great risk of smoking 1+ packs of cigarettes per day compared to heterosexual men and women, respectively. Among those who had never used marijuana, gay men (aOR=0.51[95%CI=0.36,0.72]), bisexual men (aOR=0.69[95%CI=0.50,0.95]), gay/lesbian women (aOR=0.47[95%CI=0.34,0.65]), and bisexual women (aOR=0.43[95%CI=0.35,0.51]) were significantly less likely to perceive great risk of marijuana use once per month compared to heterosexual men and women, respectively. Similar results were found for perceiving great risk of using marijuana 1-2 times per week.
Conclusions: As perceived risk is a strong and consistent risk factor for initiation of tobacco and marijuana, our findings of significantly lower risk perceptions among sexual minority young adults suggests they may be at increased risk of tobacco and marijuana use initiation during this age period.
Financial Support: This work was supported by the National Institute on Drug Abuse and the US Food and Drug Administration (FDA) Center for Tobacco Products (R21DA051388).

M22. Validating Self-Reported Electronic Nicotine Delivery System Use With Biochemical and Topographical Measures

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: Quick, self-reported estimates of cigarette smoking have been vital in understanding the health impact of smoking. A major challenge to understanding the effects of long-term ENDS use on health is the absence of a systematic method of quantifying ENDS use. This preliminary study measured nicotine and its metabolites as biomarkers of ENDS use in order to validate self-report estimates.
Methods: 30 young adults who currently use ENDS completed a 7-day time-line follow-back and an ENDS ad lib topography session. Participants submitted urine, and had blood drawn before and after the topography session. These samples were analyzed for nicotine and its metabolites.
Results: Tobacco/ENDS use was quantified by summing the number of occasions/hours of ENDS use and the number of other tobacco products. Partial correlations were performed between the nicotine biomarkers and the time-line follow-back sums, using urine nicotine metabolite ratio (NMR) as a covariate of no interest. The 1-back correlated with cotinine levels ($r = .383$, $p = .040$). Partial correlations were performed for blood nicotine boost (pre- to post-topography session) and topography measures, using the delay to the second blood draw and the urine NMR as covariates of no interest. The strongest correlation was with total puffing time ($r = .589$, $p < .001$). Participants reported taking 20 ± 14 puffs during the session, which was significantly lower than the actual number of puffs measured by topography (36 ± 23 puffs, $p < .001$). Both average puffing volume and puffing duration were positively correlated with FTND and NMR.
Conclusions: These results suggest that participants' recall of their occasions/hours of ENDS use is an accurate estimate of nicotine exposure, and that participants underestimate their number of puffs. Further

studies are necessary to test the veracity and reliability of these self-reports, e.g., by comparing self-reported recall to an objective measure of ENDS use.
Financial Support: Medical Research Endowment Fund from the University of Arkansas for Medical Sciences and by the Arkansas Biosciences Institute, the major research component of the Arkansas Tobacco Settlement Proceeds Act of 2000.

M23. An Exploratory Analysis of Tobacco Use and Demographic Characteristics Among Treatment-Seeking Adult Dual Users Who Prefer to Quit Cigarettes Only Vs. Cigarettes and E-Cigarettes Simultaneously

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Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Electronic cigarettes (EC) are now the second most popular nicotine product behind tobacco cigarettes (TC) and approximately half of EC users also smoke TCs (i.e., dual users). Most dual users intend to quit TCs, but little is known about individuals who plan to quit both ECs and TCs simultaneously versus those who plan to quit TCs only and continue using ECs.
Methods: Data are from an interim analysis of an ongoing, national randomized controlled trial of cessation treatment for adults who smoke TCs daily and used ECs in the past month. We explored demographic and tobacco use characteristics as predictors of preference for quitting TCs only, quitting both TCs and ECs simultaneously, or having no preference using backward elimination in a multinomial logistic regression model.
Results: Participants (N = 602) were 64.3% female, 83.4% white, mean = 30.0 (SD=10.6) years old, and 12.1% had less than a high school degree. Participants smoked a mean of 15.2 (SD=9.6) TCs per day and 54.1% used ECs daily in the past month. Compared to having no preference, participants were more likely to prefer quitting both TCs and ECs if they were more educated (college vs < high school degree, OR = 2.5, 95% CI= 1.01, 6.3) and older (5-year units, OR = 1.14, 95% CI = 1.01, 1.2). Compared to quitting both products simultaneously, daily EC use was associated with preferring to quit TCs only (OR = 1.9, 95% CI = 1.2, 2.9) or having no preference (OR = 1.5, 95% CI = 1.02, 2.2).
Conclusions: Age, education, and frequency of EC use may be important predictors of motivation to quit one versus both products among dual users. Future research is needed to test the clinical implications of quitting one versus both products and adapt cessation treatments accordingly.
Financial Support: T32

M24. Assessment of Actual Use Behavior for Flavored Nicotine Pouches Relative to Original Nicotine Pouches

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Drug Category Nicotine/Tobacco
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Empirical evidence regarding the potential impact of flavors in tobacco products on actual use behaviors is scarce. This study aimed to assess whether the use of flavor varieties (i.e., Berry, Cinnamon, Citrus, Coffee, Mint, and Wintergreen) may be associated with changes in on!® nicotine pouch (NP) consumption than use of the Original products using data from a longitudinal study.
Methods: Adult cigarette smokers (AS, n=399), dual users of cigarettes and smokeless tobacco (DU, n=395), and smokeless tobacco users (STU, n=353) received NP products to use under ad libitum conditions for 6 weeks. Daily diaries captured the number of pouches used and duration in the mouth for each NP flavor and nicotine level, as well as smoking and smokeless tobacco (ST) use behaviors. Mixed-effects generalized linear models were used to estimate associations between the use of each flavored product (vs. Original) and use behaviors.

Results: No statistically significant differences were observed in the total number of NPs consumed per day or total minutes the NPs were kept in mouth per day across all three user groups and six flavor varieties as well as for comparisons between the flavor varieties and the Original product, except that Mint and Wintergreen were associated with greater total minutes kept in the mouth per day among AS (model estimate=7.43 minutes; 95% CI=2.34 to 12.51 for Mint) and DU (estimate=7.60 minutes; 95% CI=2.35 to 12.85 for Wintergreen), respectively, representing an increase of ~1.4 minutes in the mouth per use occasion. Smoking and ST use behavior were comparable between users of flavored and Original products, except for a few inverse associations (e.g., STU of Coffee flavored products were less likely to use ST; OR=0.34; 95% CI=0.19 to 0.60).
Conclusions: Our results suggest that use of flavored NPs is not associated with meaningful changes in NP consumption.

M25. Graphic Images for Cigarette Packs: Effects on Cigarette Purchases and Ventilation Status

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Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: In March 2020, the Food and Drug Administration established eleven new health warnings for cigarette packages. This study investigated how health warnings influence cigarette package preferences among smokers of lower- and higher-ventilated (≤ 10% and ≥ 20% ventilation, respectively) cigarettes.
Methods: A crowdsourced sample of smokers (n=2,107; 58% males) were randomized to one of twelve groups (eleven health warnings and unlabeled control). In a discrete choice task, participants completed 9 choice trials in which they indicated whether they prefer to purchase a labeled or unlabeled cigarette package, while the latter increased in price. In a heatmap question, participants clicked on the image where they felt their attention was most strongly attracted.
Results: Significant differences in location of visual attraction were observed among the labels (p=0.001). Peripheral vascular disease (53%) and neck disease (54%) labels had the lowest proportion of participants looking inside the label and were not significantly different from control (ps>0.114). Lung disease (68%) and chronic obstructive pulmonary disease (66%) labels had the highest proportion of participants looking inside the label and were significantly different from control (ps<0.001). Moreover, a significant interaction between location of visual attraction and label was observed in the estimated price of switching to the labeled package (p=0.003). Participants who clicked outside the label switched to the labeled package at higher prices (p<0.001). A significant additive effect of ventilation status was observed (p=0.015) with smokers of lower-ventilated cigarettes being more resistant to purchasing packaging with health warning labels.
Conclusions: This study suggests that smokers prefer warning labels with less repellent images. Moreover, the cigarette health warnings may differentially impact individuals who smoke lower- and higher-ventilated cigarettes, with lower-ventilated cigarette smokers being more repulsed by health warning labels.
Financial Support: National Institutes of Health, National Cancer Institute grant (5P01CA217806)

M26. Prevalence and Correlates of Tobacco-Free Oral Nicotine Product Use Among Adolescents in Southern California

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To examine prevalence of tobacco-free oral nicotine product use in relation to other tobacco products and examine differences by sociodemographic factors and tobacco product use among adolescents in Southern California.

Methods: In this cross-sectional study, adolescents in 9th or 10th grade from 11 high schools in Southern California were surveyed about their nicotine and tobacco use between September-November 2021. We examined prevalence of self-reported ever and past 6-month use of nicotine pouches, other oral nicotine products (i.e., gum, lozenges, and/or gummies), e-cigarettes, combustible cigarettes, hookah/waterpipe, cigars, cigarillos, and snus. We additionally we examined whether sociodemographic factors and tobacco-product use correlate with use of tobacco-free oral nicotine products.
Results: Prevalence of ever use was 9.6% for e-cigarettes, 3.1% for nicotine gum, lozenges, and/or gummies, 2.0% for any combustible tobacco product, 0.6% for nicotine pouches, and 0.3% for snus. Prevalence of past 6-month use was 5.5% for e-cigarettes, 1.4% for nicotine gum, lozenges, and/or gummies, 1.3% for any combustible tobacco product, 0.3% for nicotine pouches and 0.3% for snus. Ever use of tobacco-free oral nicotine products was 43.4% among dual users of e-cigarettes and combustible tobacco, 29.4% among exclusive users of combustible tobacco, 22.2% among exclusive users of e-cigarettes, and 0.83% among never users of e-cigarettes or combustible tobacco. Use of any tobacco-free oral nicotine product was greater for Hispanic (vs. all other races/ethnicities except for Asian, adjusted OR [aOR]: 2.4, 95% CI: 1.3-4.4), gender minority (vs. male, aOR: 2.3, 95% CI: 1.2-4.6), female (vs. male, aOR: 1.9, 95% CI: 1.2-3.0), and sexual minority participants (vs. heterosexual, aOR: 1.6, 95% CI: 1.0-2.4).
Conclusions: Tobacco-free oral nicotine products were the second most prevalent nicotine product used by adolescents in Southern California in Fall 2021. Surveillance of tobacco-free oral nicotine products should be a national policy and public health priority.
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M27. Racial Disparities in Awareness of Cigar Health Warnings by Cigar Type

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Racial/ethnic minorities are more likely to smoke certain types of cigars and perceive them as less harmful to health. It is unclear if these disparities are related to awareness of health warnings on cigar products. Our study aimed to understand racial disparities in awareness of cigar warning labels by cigar type (traditional, cigarillos, and filtered cigars).
Methods: Data are from adults surveyed in Wave 4 (2017) of the Population Assessment of Tobacco and Health Study, a nationally representative cohort of U.S. residents aged 18 or older (n=33,643). We examined whether adults in the past month were aware of cigar warning labels and how closely current cigar users read or looked closely at them on packages of traditional, cigarillo, and filtered cigar products. Weighted proportions and chi-square tests were performed to estimate associations between race and awareness of health warnings for each cigar type.
Results: Black adults were more likely than Whites to notice warning labels on cigarillos (33% vs. 18%), traditional (27% vs. 18%), and filtered cigars (28% vs. 13%). Black cigar smokers were more likely than Whites to “often/ very often” read and look closely at warning labels on cigarillo (24.9%, vs. 13.4%, respectively; chi-sq = 25.5, df = 6; $p<0.01$) and traditional cigar packaging (23.5% vs. 8.4%; chi-sq = 14.9, df = 6; $p=0.02$), but differences for filtered cigars was not statistically significant (25.1% vs. 18.2%; chi-sq = 12.7, df = 6; $p=0.05$).
Conclusions: Preliminary findings suggest that Blacks are more likely to notice warning labels on cigar products and look more closely at them on cigarillos and traditional cigars. Future research will explore relationship between disparities in awareness of cigar warning labels, cigar use patterns, and possible confounding factors.

M28. Risk Factors Associated With E-Cigarette Use Among Adults in North Central Florida

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: While e-cigarette usage has become an important public health concern in the United States, risk factors for its use are still not fully understood. The purpose of this analysis is to assess common risk factors for lifetime e-cigarette use. We hypothesized that higher e-cigarette use would be associated with being White, male, having history of asthma, having no access to care, and having poor general health.
Methods: The sample of 2,721 adults aged 25 to 50 were interviewed between 2014 and 2021 with the Community Health Needs Assessment survey of HealthStreet, a community engagement program of UF's Clinical and Translational Science Institute. Logistic regression models were used to estimate odds ratios and 95% confidence intervals.
Results: In this sample, the lifetime prevalence of e-cigarette use was 21.0% (n=578); the lifetime prevalence of asthma was 22.0% (n=600). Being male was a risk factor for e-cigarette use (OR=1.468, 95% CI=1.162, 1.854). History of asthma was a protective factor against e-cigarette use (OR=0. 724, 95% CI=0.558, 0.942). Compared to Other individuals, Whites were nearly twice as likely to use e-cigarettes (OR=1.763, 95% CI=1.166, 2.664) while Blacks were much less likely (OR=0.401, 95% CI=0.261, 0.618). Neither access to care nor general health were significantly associated with e-cigarette use.
Conclusions: Inconsistent with our hypothesis, history of asthma was associated with lower risk of e-cigarette use while no access to care and poor general health were not associated with e-cigarette use. Consistent with our hypothesis, being White and male were associated with higher risk of e-cigarette use.
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M29. Social Media Use and Subsequent E-Cigarette Susceptibility and Initiation Among US Adolescents: Results From the Population Assessment of Tobacco and Health (PATH) Study Waves 4 (2016-2018) and 5 (2018-2019)

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Drug Category Nicotine/Tobacco
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: E-cigarette use is commonly portrayed on social media (e.g., ads, posts from e-cigarette using peers, influencer endorsements). Previous studies showed associations between social media use and youth e-cigarette use. However, there is a paucity of longitudinal studies examining the influence of social media use on e-cigarette use behaviors, such as susceptibility to use, ever and current use. We examined the longitudinal association between social media use and e-cigarette use intentions/behaviors using US nationally-representative sample of youth.
Methods: We analyzed youth data from the Population Assessment of Tobacco and Health (PATH) Study Waves 4 (2016-2018) and 5 (2018-2019). Among those who never used e-cigarettes at Wave 4 (N=7,872), we used a multivariable multinomial logistic regression to examine the associations between social media use at Wave 4 (never, nondaily, daily) and e-cigarette use behaviors at Wave 5 (non-susceptible never use [Ref], susceptible never use, ever use, current use), after controlling for other associated factors (e.g., demographics, peer/parental e-cigarette use, risk perceptions of e-cigarettes).
Results: Among the analytic sample, 10.4%, 11.4% and 78.3% reported never, non-daily and daily use of social media at Wave 4, respectively. In the adjusted regression model, daily social media use (vs. never) was significantly associated with susceptibility to e-cigarette use (aRRR=2.01; 95% CI=1.54, 2.61), as well as, ever use (aRRR=2.33; 95% CI=1.58, 3.43) and current use of e-cigarettes (aRRR=1.77; 95% CI=1.23, 2.55). We did not find significant differences in e-cigarette use intentions/behaviors between never and non-daily social media use.

Conclusions: Daily social media use among youth who had never used e-cigarettes was associated with increased susceptibility to e-cigarette use, ever and current use of e-cigarettes, one year later. Given that youth use social media on a daily basis, efforts to curtail e-cigarette-related content on social media as well as prevention and education efforts directed at youth and parents are urgently needed.
Financial Support: The research reported in this publication was supported by grant number U54DA036151 and R01DA049878 from the National Institute on Drug Abuse (NIDA) and U.S. Food and Drug Administration (FDA) Center for Tobacco Products (CTP)

M30. Tobacco Free Nicotine E-Cigarette Use Among Young Adults

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Drug Category Nicotine/Tobacco
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: E-cigarettes advertised to contain tobacco free nicotine (TFN), meaning synthetic nicotine rather than tobacco derived, are becoming increasingly available. It is unclear if TFN can be regulated like tobacco products. Little is known about TFN product use, specifically in groups at risk for vaping, like young adults. The current study examined e-cigarette use behaviors among young adults who do and do not report TFN e-cigarette use.
Methods: U.S. young adults (18-25) reporting ever e-cigarette use were recruited via online panels in Fall 2021 (n=927) and answered questions about TFN and non-TFN products. Participants were categorized by ever use of TFN e-cigarettes (yes, n=317 [34.2%]; no, n=610 [65.8%]). Bivariate comparisons by TFN vaping status were used for demographics, e-cigarette devices (e.g. JUUL, disposables), and flavor types (e.g. fruit, mint). Binary logistic regressions were used to examine whether frequency of past 30-day vaping, lifetime vaping experiences (<100 times vs. ≥100 times), and other tobacco product (combustible, smokeless, pouches, hookah, all entered separately), cannabis, or alcohol use were associated with TFN vaping.
Results: Young adults reporting TFN vaping were younger and more likely to be Non-Hispanic White. Compared to non-TFN users, a higher proportion of TFN vapers reported having tried most e-cigarette device and flavor types. In adjusted models, more frequent past-30 day vaping and lifetime vaping (>100 times) was associated with greater likelihood of TFN vaping (respectively, aOR: 1.03, 95%CI:1.01,1.04; aOR: 2.14, 95%CI: 1.56,2.94, ps < .001). Among products, only nicotine pouch use was associated with greater odds of TFN vaping (aOR:1.90, 95%CI:1.14,3.17, p<.01).
Conclusions: Young adults with more frequent e-cigarette use were more likely to use TFN e-cigarettes. Interestingly, nicotine pouches, which advertise TFN formulations, were associated with TFN vaping. Given the increased prevalence of TFN products on the market, it is important to examine use and appeal among young adults.
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M31. Young Adults' Interest in Using Tobacco-Free Nonmedicinal Oral Nicotine Products to Quit Vaping

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Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research

Aim: Flavored tobacco-free oral nicotine products, including nonmedicinal nicotine gums, lozenges, gummies, or pouches, may be attractive means to quit vaping among young adult e-cigarette users who otherwise struggle to quit using e-cigarettes. This study aimed to examine associations of interest in using tobacco-free oral nicotine products to quit vaping with e-cigarette use history and characteristics among young adult e-cigarette users.
Methods: Using data from a cohort originally recruited as teens in Los Angeles, cross-sectional web-based survey responses collected in 2021 were analyzed among young adult past 30-day e-cigarette users [n = 148; mean age (SD) = 21.8 (0.4); 54.7% female] who reported having seriously considered quitting vaping within the next 6 months. Participants self-reported e-cigarette use history and interest in using tobacco-free oral nonmedicinal nicotine products (yes/no) and several FDA-approved tobacco use cessation medications to quit vaping (yes/no).
Results: Respondents' interest in using flavored tobacco-free oral nonmedicinal nicotine products (46.6%) to quit vaping was higher than interest using either medicinal nicotine gum/lozenges (25.8%), nicotine transdermal patch (19.0%), or prescription medications (17.0%) to quit vaping. Interest in using flavored tobacco-free oral nicotine products to quit vaping was associated with vaping ≥20 vs. <10 days in the past month (OR = 3.20, 95% CI = 1.37 – 7.77), vaping ≥10 vs. <10 times per day during vaping days (OR = 2.46, 95% CI = 1.13 – 5.51), and low vs. high self-efficacy in ability to quit vaping (OR = 3.53, 95% CI = 1.55 – 8.41).
Conclusions: In young adult e-cigarette users, using flavored tobacco-free nonmedicinal oral nicotine products may be attractive means to quit vaping among those motivated to quit vaping, particularly for frequent vapers with low quit self-efficacy. Further studies are needed to determine whether young adults who take up tobacco-free oral nicotine products successfully stop vaping.
Financial Support: Research reported in this publication was supported by the National Cancer Institute and the FDA Center for Tobacco Products (CTP) under Award Number U54CA180905, National Cancer Institute under award number R01CA229617, National Institute on Drug Abuse under award number K24DA048160, and the National Heart, Lung and Blood Institute (K01HL148907). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the FDA.

M32. Clouding up Cognition: Secondhand Cannabis and Tobacco Exposure Related to Cognitive Functioning in Youth

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Drug Category Other, Cannabis and Tobacco
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Increasing legalization of cannabis, in addition to longstanding rates of tobacco use, raise concerns for possible cognitive decrements from secondhand or environmental (after smoke dissipates) exposure to smoke. Yet few studies have investigated the impact of secondhand cannabis, particularly in youth. We investigate the relation between cognition and secondhand and environmental exposure to cannabis and tobacco.
Methods: The Adolescent Brain Cognitive Development (ABCD) Study Year 2 Follow-Up was used (n=5,580; 48% Female; 10-13 years-old), including performance across cognitive measures and parent reported secondhand or environmental cannabis or tobacco exposure. A principal components analysis was run to identify latent factors. Linear mixed effects models assessed cognitive performance on a global cognition component and individual tasks by cannabis and/or tobacco environmental exposure. Sociodemographics and other potential confounds (e.g., prenatal exposure) were also examined. P-values were adjusted using the false-discovery rate method.
Results: A global cognition component was identified. Secondhand ($p<.001$) and environmental tobacco exposure ($p<.001$) was related to lower global cognition while environmental cannabis exposure ($p=.03$) was related to higher global cognition compared to no exposure, but no results remained significant after inclusion of covariates. Beyond covariates and family- and site-level factors, secondhand tobacco was

related to poorer visual memory (p=.02), environmental tobacco was associated with poorer visuospatial (p=.02) and language skills (p=.008). Environmental cannabis was related to better oral reading (p=.01).
Conclusions: Parent reported secondhand tobacco exposure was associated with poorer visual memory and overall global cognition, while environmental tobacco exposure was related to poorer language, visuospatial skills, and global cognition. Secondhand cannabis was not related to cognitive functioning after controlling for sociodemographic factors, but environmental cannabis exposure was related to better oral reading and increased global cognition. As this is the first known study of its kind, secondhand cannabis should continue to be investigated to confirm results.
Financial Support: K08DA050779 PI: Wade, N.E; U01DAO41025 PI: Lisdahl, K.M.

M33. Craving: An Early and Predictive Marker of Addiction? Baseline Results of a Prospective Study

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Drug Category Other, Alcohol, Tobacco and cannabis
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Craving, defined as an intense and unwanted desire to use, could play a key role in Substance Use Disorders (SUD). Craving is both one of core diagnosis criterion for SUD in DSM-5 and also a dynamic phenomenon with daily variations that are prospectively associated with use. These characteristics give to craving a prognostic and etiologic value in addictive disorders. Among all DSM-5 diagnostic criteria for SUD, Item Response Theory (IRT) analysis have shown that craving was the most frequent and discriminant criterion and Network Analysis have shown that craving is the more central criterion. Also, the presence of craving in subjects with mild severity SUD suggest that it could be among the earliest symptom to appear, making craving a candidate early marker of addiction. The main objective of this study was to explore whether craving was an early marker of addiction.
Methods: This ongoing prospective longitudinal one-year follow-up study included current regular users of tobacco, alcohol or cannabis, that screened negative on the Cut down, Annoyed, Guilty, Eye Opener (CAGE) or Cigarette Dependence Scale (CDS) screening interviews. The DSM-5 SUD criteria were assessed at inclusion and then every 3 months.
Results: Among the current 28 subjects included, 50% male (n=14) and an average age of 45 years (SD=14.06), the main substance was alcohol (71%, n=20). Analyses of baseline data show that among users 32% reported craving for the inclusion substance (n=9) and all meet another criteria for SUD making craving a better and early marker than CDS or CAGE screening.
Conclusions: Presence of craving in regular users could be better predictive for SUD that screened negative CAGE or CDS.
Financial Support: Institut National du Cancer et Institut pour la Recherche en Santé Publique

M34. Fluctuations of Clinical Insight in Daily Life Influences Craving Intensity in Addiction

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Drug Category Other, substances and behaviors
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Clinical insight and craving seem to be related, at between-person level, among individuals with addiction. Using Ecological Momentary Assessment (EMA), craving has been shown to fluctuate over time, at within-person level, and this may also be possible for clinical insight. Our aim was to examine if insight fluctuates on a daily basis at the within-person level, and the influence of such fluctuations on craving intensity, response to cues, and use in daily life using EMA among individuals with addictions.
Methods: 39 participants were recruited from outpatient addiction clinics and harm reduction services in France. They completed a 14-day EMA protocol to capture momentary craving and clinical insight, with the

Momentary Clinical Insight Scale (MCIS). Data were analyzed using Hierarchical linear and nonlinear modeling (HLM).
Results: Variance of insight in daily life was composed by 18.8% of within-person variance. A decrease of clinical insight was strongly associated with a decrease of craving intensity self-reported at the next assessment, even after adjustment on craving at T0 ($\gamma = 0.212$, $p < 0.001$), which remained significant ($\gamma = 0.261$, $p = 0.007$) after adjustment on age, sex, education, addiction type and severity, average level of craving and insight, craving and use at T0. Higher craving intensity was also associated with higher concurrent ($\gamma = 0.096$, $p < 0.001$) and later ($\gamma = 0.014$, $p = 0.046$) level of insight, adjusted on insight at T0. Insight was not found associated with number of cues nor use reported in daily life.
Conclusions: Clinical insight presented within-person variations at daily level. Momentary decrease of clinical insight was prospectively and bidirectionally linked to a decrease of craving intensity reported in the following hours. Future studies are needed to further investigate and better understand how clinical insight impacts craving, use, and relapse.
Financial Support: Nouvelle-Aquitaine region (N°APE01083; N°2017 – 1R30114) and Institut de Recherche en Santé Publique (IRESP) (N°IRESP-19- ADDICTIONS-16).

M35. Delay Discounting Predicts Remission Mediated by Regulatory Flexibility in Substance Use Disorder Recovery

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Drug Category Other, Recovery from 1+ substance use disorder
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: Delay discounting (DD) and coping are robust predictors of substance use disorder (SUD) outcomes. Further, regulatory flexibility (flexibly using coping techniques based on contextual demands) is related to psychological resilience. However, few studies have investigated the relationship between DD and regulatory flexibility amongst individuals in recovery from SUD.
Methods: Ninety-three individuals in SUD recovery (67 in remission [not meeting DSM-5 criteria for any SUD]) completed self-report questionnaires to assess regulatory flexibility and completed an Adjusting Amount Delay Discounting Task. T-tests were used to examine differences in regulatory flexibility and DD by remission status. Pearson correlations were used to examine the relationship between regulatory flexibility and DD. A mediation model was used to examine the relationship between DD, perceived ability to cope with trauma (PACT; including flexibility and forward and trauma focused coping), and remission.
Results: Remitted individuals had significantly lower DD rates ($p=0.042$) and higher perceived ability to cope with trauma ($p=0.014$) compared to non-remitted individuals. Moreover, DD significantly correlated with context sensitivity (presence: $p=0.00046$; absence: $p=0.00417$), flexibility ($p=0.0127$), and perceived ability to cope with trauma ($p=0.0331$). Finally, the Forward Focus domain of the PACT Scale significantly mediated the relationship between DD and remission status ($p=0.040$).
Conclusions: Results suggest remitted individuals have broader temporal windows compared to non-remitted individuals and individuals in recovery with a broader temporal window are better able to identify contextual demands and flexibly regulate their emotions. Finally, the mediation results suggest having a broader temporal window influences ability to remain focused on future goals and plans, contributing to sustained remission in recovery.
Financial Support: Fralin Biomedical Research Institute

M36. Diminished Error-Related Negativity and Error Positivity in Adults With Addiction Problems and Disorders: A Meta-Analysis on Error Processing

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Drug Category Other, Subclinical and Clinical Addiction
Topic Imaging

Abstract Detail Human
Abstract Category Literature Review
Aim: Deficits in error processing are reflected in the inability of individuals with externalizing problems, such as patients with an addiction disorder, to adjust their problem behavior. The present poster displays results of a larger meta-analysis, testing whether error processing indexed by the event-related potentials error-related negativity (ERN) and error positivity (Pe) are reduced in adults with addiction problems or disorders when compared to healthy controls.
Methods (Optional): A systematic search was conducted in PubMed (1980-Dec. 2018), PsychInfo (1880-Dec. 2018) and Scopus (1970-Dec. 2018) identifying 328 studies. Studies measuring error processing using the Eriksen Flanker, the Go-NoGo or the Stop-Signal task, in adults or children with clearly described externalizing behavioral problems (e.g., aggression) or a clinical diagnosis within the externalizing spectrum (e.g., addiction), and healthy controls were included. Only results of individuals with addiction problems and addiction disorders, including cannabis, alcohol, tobacco, heroin, cocaine, food and gaming will be presented.
Results (Optional): Random effects model for ERN at the frontal-central electrode (K= 13 studies; 734 subjects) revealed a reduced ERN (Hedges's g = 0.49, 95% confidence interval [CI] .22, .76) for patients with addiction problems or disorders compared to healthy controls. For Pe at the central electrode (K=12 studies, 714 subjects), a reduced amplitude was found (Hedges's g = -0.06, 95% CI -.27, .16), suggesting diminished error processing in individuals with addiction problems or disorders as compared to healthy controls. Moderation analyses for the presence of performance feedback, comorbidity, electrode site and employed cognitive task for both ERP's will be displayed. Small sample assessment revealed no evidence of publication bias for both ERP's.
Conclusions: Not all moderators did explained the potential heterogeneity in most of the analysis suggesting that other disorder and patient specific related aspects affect error processing. The results indicate the presence of a compromised error processing in individuals with addiction problems, proposing diminished prefrontal cortical activation during performance monitoring
Financial Support: Erasmus Initiatives for Vital Cities and Citizens, Erasmus University Rotterdam, the Netherlands

M37. Predicting Choice From Response Latencies: A Potential Treatment Target for Behavioral Allocation Disorders

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Drug Category Other, Food reinforced behavior
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Understanding how choices are made could aid in preventing harmful choices and encouraging healthy choices. This experiment compares two models of choice: Rational Choice Theory (RCT) and the Sequential Choice Model (SCM). In RCT, choice between the same item is based on cost with the lowest cost option being chosen. In the SCM, the option with the shortest response latency when each is presented alone is chosen.
Methods: In these experiments, food-reinforced behavior in 16 female Lewis rats was observed under three high-cost conditions (FR10, FR20, FR40) with the low-cost condition always being FR5. Two levers with varying high or low cost were presented either simultaneously or independently. The latency to the first response on each lever in each trial, as well as the number of fixed-ratios completed on each lever were recorded. The relationship between latency to choose the right versus left lever during simultaneous or independent lever presentations was determined for each contingency condition by linear regression. Subjects were then administered separate pretreatments of amphetamine and pentobarbital to assess the pharmacological effects on this relationship.
Results: The probability of shorter response latency for independently presented options significantly predicts the pattern of responding when both options are simultaneously available. The relationship was strongest when the high-cost condition was FR10 (R2=0.8) or FR20 (R2=0.7); and was not greatly affected by amphetamine or pentobarbital pretreatments.

Conclusions: The latency to respond for reinforcement in isolation may predict choice when two options are simultaneously available, i.e., choice was better predicted by the SCM than by RCT. One implication of this is that increasing the latency to respond for a problematic outcome or decreasing the latency to respond for more healthful outcome may make healthy choices more frequent.
Financial Support: NIAAA Grant AA025664

M38. Population Exposure to Marijuana and Illicit Drugs is Increasing While Exposure to Prescription Pain Relievers is Decreasing in the United States

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Drug Category Other, Multiple drug classes
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The number of individuals using drugs and the number of days using both contribute to the overall exposure of the national population to drug use risks. Combining both metrics into person-days of exposure provides a meaningful metric of how frequently drugs are used by the population. This study quantifies the change in person-days of exposure by examining the National Survey on Drug Use and Health (NSDUH).
Methods: Use/misuse in the past month was examined for marijuana, illicit drugs (methamphetamine, hallucinogens, heroin, cocaine, crack), and prescription drugs (pain relievers, stimulants, tranquilizers, and sedatives) in NSDUH between 2015 and 2019. Total person-days of exposure, number of people, and median number of days were estimated for each drug.
Results: The number of past month person-days of exposure increased for marijuana (319M person-days to 474M; 48% increase) and illicit drugs (34M to 45M; 35% increase) while decreasing for prescription drugs (47M to 41M; 14% decrease). Marijuana exposure increased in number of people (22M to 32M) and median number of days (10.0 to 12.0). The primary increase in exposure to illicit drugs was from methamphetamine, where number of people using increased from 0.8M to 1.2M and median number of days increased from 8.7 to 14.0. Number of people using hallucinogens also increased from 1.2M to 1.9M; median number of days stayed at 1.0. Decreases in number of people misusing pain relievers (3.7M to 2.8M) were partially offset by increasing median days of misusing sedatives (2.1 to 4.8).
Conclusions: Total exposure to drug use is increasing in the US, primarily from marijuana, methamphetamine, and hallucinogens. As prescription drug use is decreasing, the US population is more at risk of adverse events involving illicit drugs, such as overdose from fentanyl adulterants. Use of illicit drugs and marijuana have become a dominant public health concern over prescription drug misuse.
Financial Support: The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado. The RADARS System is supported by subscriptions from pharmaceutical manufacturers, government and non-government agencies for surveillance, research and reporting services. Subscribers did not participate in data collection or analysis of this abstract.

M39. An Online Survey of the Impact of the COVID-19 Pandemic on Drug and Alcohol Use, Employment, and Mental Health

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Drug Category Other, Multiple Substances
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To assess the effect of the COVID-19 pandemic on substance use, employment, and mental health among the adult general population in the United States.
Methods: A convenience sample of adults living in the United States completed an anonymous online survey between July 2020 and February 2021. Respondents provided information on demographics,

substance use, employment, mental health, exposure to COVID-19, and how these and other lifestyle measures were affected by the COVID-19 pandemic.
Results: The survey was completed by 380 adults, mean age 41.4 (SD=12.6). Most respondents identified as White (93%), most identified as female (78%), half had a post-graduate degree (50%), most were employed full-time (56%), and the plurality were from Maryland (40%). In the 30 days prior to completing the survey, 16% of respondents smoked at least part of a cigarette, 72% had at least one alcoholic beverage, and 30% used a cannabis product. Other substances that more than 2% of respondents reported using in the previous 30 days included psychedelics, prescription painkillers, prescription tranquilizers, MDMA, and powder cocaine. During the pandemic, 19% of respondents experienced a change in employment status or hours. 23% of smokers, 61% of alcohol users, 58% of cannabis users, and 42% of other drug users reported increased use during the pandemic—significantly higher proportions than those reporting decreased use for each category. Many respondents also indicated that they had exposed themselves to risk of contracting COVID-19 to obtain tobacco, alcohol, cannabis, or other substances. Finally, nearly all respondents reported mild, moderate, or severe pandemic-related stress.
Conclusions: Most respondents reported increased stress due to the pandemic, and respondents were more likely to report an increase in substance use than decreased use. These outcomes are consistent with previous findings and highlight the need for greater treatment and support as the COVID-19 pandemic continues.
Financial Support: T32DA07209

M40. Effects of the COVID-19 Pandemic on New Cases of Drug Diversion in the United States

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Drug Category Other, Prescription Medications
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Most individuals who nonmedically use prescription medications report they acquired a drug by diversion, the transfer of prescription drugs from a lawful to an illegal channel. The effects of the COVID-19 pandemic on prescription drug diversion remain unknown. This study examines the effect of the COVID-19 pandemic on the number of new drug diversion cases recorded by law enforcement agencies in the United States.
Methods: Data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System Drug Diversion Program were used. In this program, police and regulatory agencies complete a quarterly, cross-sectional, self-administered survey to report the number of new diversion cases that occurred within their jurisdiction in the previous quarter. The number of agencies that participated per quarter ranged from 193 in 2021Q2 to 216 in 2019Q3. The average number of new diversion cases per questionnaire were compared across two periods: pre-COVID (2018Q1-2019Q4) and post-COVID (2020Q1-2021Q2), using a negative binomial regression.
Results: The average number of new diversion cases reported by agencies decreased by 35.3% (95% CI: 28.0%-41.8%, $p<0.001$) from an average of 9.1 new cases per survey (95% CI: 8.5-9.7, $p<0.001$) in the pre-COVID period to an average of 5.9 new cases per survey (95% CI: 5.4-6.4, $p<0.001$) in the post-COVID period. 49.2% of diversion cases involved prescription opioids and 9.3% involved prescription stimulants. The conclusion did not change after adjusting for population covered by participating agencies and number of officers working on prescription drug diversion per agency.
Conclusions: There was a substantial decline in new drug diversion cases in the US during the post-COVID period. However, further research is needed to determine whether this finding reflects decreased diversion of medications, changes in law enforcement efforts, or continued increases in the use of illegal substances during the pandemic.
Financial Support: The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado. The RADARS® System is supported by subscriptions from pharmaceutical manufacturers, government and non-government agencies for surveillance, research and reporting services. Subscribers do not participate in conception, data collection, analysis, drafting, or interpretation of this abstract.

M41. Religiosity, Spirituality and Substance Use Disorders in Young Adulthood: A Developmental Approach

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Drug Category Other, Alcohol, Cannabis, and Illicit
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: 1. Test the cross-sectional association of young adult religiosity/spirituality (R/S) and substance use disorders (SUD).
2. Test the longitudinal association of family R/S and young adult SUD.
3. Test whether concordance between family and young adult R/S is associated with young adult SUD.
Methods: Across two waves, an epidemiologic sample of Puerto Ricans living in New York City or Puerto Rico provided data. In Wave 1, parents reported on family R/S (participant ages 5-17, N=2491). In Wave 2 (11-year follow-up) young adults provided self-report of R/S and current substance use (N=2004). Participants were coded Y/N for DSM-IV substance use diagnoses: alcohol dependence (AD), tobacco dependence (TD), illicit substance use/dependence (IU/D), or any SUD (ANY). Young adult R/S was coded as Devout, Engaged, Culturally Religious, Spiritual But Not Religious (SBNR), or None. Family R/S was coded as Devout, Culturally Religious, or SBNR. Family/young adult R/S concordance was coded Y/N. Logistic regression was used to test for association between variables.
Results: Statistically significant associations between young adult R/S and SUD were observed for TD, IU/D, and ANY (p=0.0015, 0.0043, and 0.0024, respectively). Devout participants were least likely to have SUDs, while SBNRs were most likely, with odds ratios of 2.685 [1.637,4.403], 2.490 [1.430,4.335], and 2.193 [1.441,3.339], respectively, in comparison to Devout. There was no significant association between family R/S and SUD. Family and young adult R/S concordance was significantly associated with TD and ANY (p=0.0003 and 0.0.0023, respectively). Family/young adult R/S Concordance predicted lower likelihood of TD and ANY, with differences in risk estimates between Y/N on Concordance of -0.0632 (-0.0965,-0.0298) and -0.6037 (-0.1046,-0.0229).
Conclusions: Devout young adults are less likely to have TD, IU/D or ANY than other R/S identities. SBNRs are most likely to have SUDs. Concordance between family and young adult R/S predicts lower risk for TD and ANY SUD.
Financial Support: National Institute for Drug Abuse; American Academy of Child and Adolescent Psychiatry

M42. The Impact of Gender-Neutral and -Specific Normative Perceptions on Substance Use and Other Risky Behavior Among Emerging Adults

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Drug Category Other, Alcohol and Cannabis
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Emerging adulthood is characterized by increased substance use and concurrent risky sexual behaviors. Research has linked general normative (mis)perceptions of these behaviors to self-reported behavior. However, there is also evidence that gender-specific normative perceptions are powerful predictors of individual substance use and sexual behavior. Despite differential impacts of gender on substance use and sexual behavior, studies have not examined whether gender-specific and non-specific normative perceptions are differentially associated with substance use and sexual behavior.
Methods: Unmarried, childless emerging adults (aged 18-25 years) enrolled in college were recruited online to complete a self-report survey (N = 389; 78% women). Participants were asked about past-month substance use and risky sexual behavior, as well as the perceived frequency of each behavior by the average adult, average man, and average woman. A series of regression-based count models were conducted to examine the relationships between normative perceptions (i.e., perceived frequency of same-gender and

gender non-specific binge drinking, cannabis use, prescription drug misuse, and risky sex acts [RSA]) and the respective self-reported behaviors.
Results: Same-gender normative perceptions were associated with binge drinking (IRR = 1.09, 95%CI: 1.05-1.14), cannabis use (IRR = 1.05, 95%CI: 1.01-1.09), and RSA (IRR = 1.46, 95%CI: 1.27-1.68). Gender non-specific normative perceptions were also associated with binge drinking (IRR = 1.04, 95%CI: 1.02-1.06) and RSA (IRR = 1.46, 95%CI: 1.27-1.68). Neither gender-specific nor gender non-specific normative perceptions were associated with prescription drug misuse.
Conclusions: Findings suggest that interventions for substance use and concurrent RSA among emerging adults that target normative perceptions (e.g., motivational enhancement therapy) should assess not only general norms, but also gender-specific norms, especially for cannabis use, for which social processes may occur more within gender. Future research should further examine the impact of social learning processes on the development of prescription drug misuse among youth.

M43. Gender-Responsive Digital Intervention for Young Adult Women With Substance Use and Co-Occurring Psychiatric Disorders

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Drug Category Other, Alcohol and other drugs
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use disorder (SUD) treatment programs that incorporate gender-responsive components have been shown to lead to enhanced treatment outcomes for women with SUDs. In a previous study, we developed a gender-responsive, digital intervention for women with SUDs as an addition to treatment as usual in mixed-gender, SUD treatment programs. For this study, we adapted the digital intervention for young adult women with substance use problems receiving mental health treatment and examined the feasibility and satisfaction of the modified digital intervention.
Methods: Women (N=44) were recruited from four inpatient and residential psychiatric treatment programs. Women were eligible for this study if they were (a) 18-25 years of age, and (b) identified by clinician as having problems with substance use. Participants engaged with the intervention on an iPad and completed pre- and post-intervention surveys assessing satisfaction with the intervention, attitudes about changing their substance use, and perception of how substance use affects their mental health.
Results: Participants were predominately White (86%) and non-Hispanic/Latina (77%); mean age 21 years (SD=2.4). On average it took participants 29.4 minutes (SD=15.4) to complete the intervention, and 80% of participants were “mostly” or “very” satisfied with the intervention. From pre- to post-intervention, participants’ interest in making changes to their substance use ($t(42) = -2.38$, $p = .02$) and their ratings of the likelihood of making changes to their substance use ($t(42) = -2.69$, $p = 0.01$) significantly increased. There were no significant changes in perception about how substance use affects their mental health.
Conclusions: These results suggest that this gender-responsive digital intervention is applicable to young women with substance use problems receiving mental health treatment. While increases in motivation to change substance use were noted, future research should examine the effectiveness of utilizing technology-based tools to address the complex co-occurrence of psychiatric illness and substance use problems in a gender-responsive way.
Financial Support: This research was funded by the Hall Mercer Endowed Chair in Child and Adolescent Psychiatry at McLean Hospital and the National Institute on Drug Abuse K23DA050780.

M44. LGBQ Microaggressions and Substance Use Among University Students: The Moderating Role of Mindfulness

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Drug Category Other, Alcohol, Cannabis, and Other Drugs (But not polyuse)
Topic Disparities
Abstract Detail Human
Abstract Category Original Research

Aim: University students with marginalized sexual orientations are at a higher risk for substance use compared to their heterosexual peers. Experiences of discrimination, such as microaggressions, have been identified as a potential contributor to this disparity. Further, mindfulness, or the ability to acknowledge one's thoughts and feelings without judgement, has been identified as a potential protective factor for discrimination among LGBQ+ people. However, limited research has examined the effect of mindfulness within the relationship between LGBQ+ microaggressions and substance use. The current study aims to better understand the relationship between sexual orientation-based microaggressions and substance use among university students, as well as the moderating role of mindfulness in this relationship.
Methods: 119 LGBQ+ university students (mean age = 19.7; 75% White; 70.5% Women; 64% Bisexual, 22% Gay, 14% Other/Blank) completed an online questionnaire that included measures assessing LGBQ+ microaggressions on campus, mindfulness, and substance use (i.e., alcohol, cannabis, and other drug use).
Results: A linear regression analysis revealed a significant relationship between on-campus LGBQ+ microaggressions and alcohol use ($\beta = .037$, $p = .028$), with a non-significant effect found for cannabis and other drug use. Moderation analyses were performed using Hayes' PROCESS Macro, finding a non-significant moderating effect of mindfulness on the association between microaggressions and each substance use outcome.
Conclusions: Findings suggests that experiencing microaggressions on campus may be a risk factor for alcohol use among LGBQ+ university students. Although a similar finding was not found for cannabis and other drug use, this may be due to the power restraints regarding sample size. Additionally, mindfulness was not found to moderate the relationship between microaggressions and substance use. However, future research should explore the effect of mindfulness in a larger LGBQ+ sample, as well as examining other aspects of psychological flexibility that could play a protective role.

M45. Gateway to Drugs: Poor School Encouragement as a Pipeline to Substance Use Disorder Among Latinx Adolescents

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Drug Category Other, All Substances
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Justice involved adolescent (JIA) minorities of color are more susceptible to substance use disorder (SUD) than their white counterparts, while also registering lower rates of treatment completion. Protective factors such as comfort in school environment and participation in school activities may increase SUD treatment completion rates among minority adolescents.
Methods: Stratified logistic regression analyses were used to examine a statewide dataset of 79,570 JIA from the Florida Department of Juvenile Justice (FLDJJ). The FLDJJ sample consisted of JIA who were arrested and administered the Positive Achievement Change Tool (PACT) intake assessment between 2004-2015. Rates of SUD, perception of school encouragement, and SUD data were obtained from the PACT and self-reported data.
Results: Preliminary results indicate that JIA youth who found school encouraging were 46 percent less likely to be diagnosed with SUD ($p < .001$). The results also indicated statistically significant racial differences as White JIA were 46 percent less likely to be diagnosed with SUD, Black JIA were 40 percent less likely to be diagnosed with SUD, and Latinx were 57 percent less likely to be diagnosed with SUD ($p < .001$). Of the 22,651 JIA that found school encouraging, 39 percent were White, 44 percent were Black, and 16 percent were Latinx.
Conclusions: The results indicate that an encouraging school environment is correlated with a lower likelihood of being diagnosed with an SUD. Particularly among Latinx students, having an encouraging school environment may represent a protective factor for preventing SUD. Latinx students are also among the lowest to report having an encouraging school environment. The data might indicate that schools with Latinx students should implement culturally and linguistically competent interventions that promote school positivity and encouragement to reduce SUD rates among the population.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely

the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

M46. Racial Differences in the Association Between Consequential Thinking and Substance Use Disorder Treatment Adherence Among Justice-Involved Adolescents

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[1]University of South Florida, [2]University of Florida
Drug Category Other, Substance Use Disorder
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Untreated substance use disorder (SUD) can devastate families and communities, especially for underserved populations. This is especially true for justice-involved adolescents (JIA) who are at a greater risk for SUD. Research has shown that a small fraction of JIA starts and completes treatment for SUD. Examining consequential thinking, individuals' understanding of consequences to their actions, is important for understanding why JIA adhere or do not adhere to the treatment programs. No study has tested the potential associations between consequential thinking and treatment adherence and whether this relationship differs by race.
Methods: Random-effect models were applied to examine a longitudinal dataset of 13,824 JIA from the Florida Department of Juvenile Justice (FLDJJ) who entered the FLDJJ between 2005-2019. The odds ratios were estimated to examine the association between consequential thinking and treatment adherence. Stratified logistic regressions were used to test racial differences in the association between consequential thinking and treatment adherence.
Results: Preliminary results show that a higher level of consequential thinking was associated with 54% higher odds of treatment adherence. Stratified models indicate that there is a stronger association between consequential thinking and treatment adherence for Black and Latinx JIA compared to White JIA. The odds of treatment adherence were 79%, for Black, 67%, Latinx, and 49%, for White, higher for individuals who believe in consequences in their actions than those who did not.
Conclusions: Findings indicate that improving consequential thinking may improve SUD treatment adherence, especially among racial/ethnic minority JIA. The development and delivery of SUD treatment for JIA would benefit from greater attention to consequential thinking as a motivational factor for JIA to continue the treatment.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

M47. Assessing Whether a Survey-Driven Tablet-Based Intervention Increased Willingness of Black Women With Substance Use to Attend a Prep Clinic Following an Emergency Department Visit

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Drug Category Other, Includes alcohol, cannabis, polysubstance use, and stimulants. Only excludes tobacco use.
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: We launched the first pilot randomized controlled trial (RCT) of a behavioral intervention, increasing PrEP (iPrEP), to increase willingness for PrEP and motivate an initial PrEP clinic visit for Black women following an emergency department (ED) visit.
Methods: Eligible participants were Black cisgender women ages 18- 55 years who acknowledged recent condomless sex and substance use. Participants were randomized to iPrEP or usual care (UC). iPrEP is a survey-based intervention designed to raise awareness and knowledge about PrEP. Participants completed an assessment of knowledge of and willingness to use PrEP before and after the intervention, then were

engaged to schedule a PrEP clinic appointment from the ED. Enrolled participants were followed for six months.
Results: Forty enrolled participants were ages 18-54 years. Education levels varied evenly between some high school and graduate school. Most participants were single (n=25) or married (n=7). Twenty-two participants were employed full-time. Pre-test results confirmed that 21/40 participants had heard of PrEP. All 40 participants affirmed PrEP as a daily HIV prevention medication. For those randomized to iPrEP, the odds of knowing about PrEP at post-test, when controlling for baseline, were higher by a factor of 5.2 relative to UC. iPrEP had no effect on willingness relative to UC. The estimate for iPrEP participants is marginally higher (4.16 vs. 4.04); however, the predicted probabilities of 67.9% does not suggest a strong degree of evidence in favor of an effect. During the post-test, those receiving iPrEP were less ready to take PrEP than those receiving UC.
Conclusions: Findings suggest that while iPrEP increased knowledge, it had no effect on willingness and a negative impact on readiness to take PrEP relative to UC. It is imperative for future research to carefully consider the way in which information about PrEP (e.g., side effects, pill burden) is delivered to cisgender Black women.
Financial Support: Gilead Sciences, Inc.

M48. Emerging Sex Differences in Adolescent Substance Use

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Drug Category Other, Multiple drugs, not concurrent use
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Adolescence is a vulnerable time for development of substance use disorders and the emergence of sex differences in substance use patterns. Although similar in early adolescence, male and female substance use patterns historically have diverged by young adulthood, with males using more substances than females. Most prior studies focused on an older cohort of individuals, have not included a nationally representative sample, and were limited to one or two substances studied, potentially missing the sentinel time during which sex differences emerge and the scope of sex differences depending on the sample utilized or the substances examined. Additionally, as cultural shifts around gender norms have occurred in the past decade, examining the emergence of sex differences with newer data is valuable. We hypothesized that certain sex-specific substance use patterns emerge as students' age increases.
Methods: Data are from the 2019 Youth Risk Behavior Survey (n=13,677), a nationally representative sample of high school students. Weighted logistic analyses of covariance adjusting for race/ethnicity compared males' and females' substance use (14 outcomes) by age category.
Results: Among all adolescents, more males reported illicit substance use and cigarette smoking than females, whereas more females reported prescription opioid misuse, synthetic cannabis use, recent alcohol use, and binge drinking. Divergence between male and female use usually occurred at 18+ years. The odds of using most illicit substances were significantly greater among males than females at age 18+ years (aORs 1.7-4.47). Among 18+ year-olds, males and females did not differ in electronic vapor product use, alcohol use, binge drinking, cannabis use, synthetic cannabis use, cigarette smoking, or prescription opioid misuse.
Conclusions: Sex differences in adolescent use of most but not all substances emerge by age 18+ years. Patterns of sex differences of adolescent substance use may inform specific prevention efforts and identify peak ages for intervention.
Financial Support: Devika Bhatia was supported by a postdoctoral training grant, Grant Number T32 MH015442.

M49. Sex Differences in Military Workplace Victimization and Drug Use Among U.S. Army Reserve/National Guard Service Members

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Drug Category Other, Any drug use
Topic Sex/Gender Differences

Abstract Detail Human
Abstract Category Original Research
Aim: Workplace victimization involves a power differential wherein the perpetrator intentionally and repeatedly physically, emotionally, or socially harms another. In civilian settings, workplace victimization is associated with a host of negative health outcomes, yet studies on workplace victimization in the unique context of military environments are scarce. This research examines workplace victimization occurring in military jobs and its associations with drug use.
Methods: Data come from Operation: SAFETY (Soldiers And Families Excelling Through the Years) an ongoing study of U.S. Army Reserve/National Guard (USAR/NG) soldiers and their spouses. The current sample was comprised of 280 current soldiers (male n=234 ; female n= 46). The Negative Acts Questionnaire-Revised (NAQR) assessed exposure to workplace victimization and includes measures for work, person, and physical bullying at the third yearly assessment. The NAQR total score was used in all models. Logistic regression models examined the relation between past year drug use and workplace victimization in military jobs. Models were run separately for males and females, and controlled for years of military service and illicit drug use norms.
Results: Past year drug use was 6.5% for female, and 9.8% for male, soldiers. For female soldiers, greater workplace victimization was significantly associated with higher odds of past year drug use (Adjusted Odds Ratio (AOR) = 1.11, 95% Confidence Interval (CI) = 1.01, 1.22). For male soldiers, greater workplace victimization was not significantly related to past year drug use (AOR = 1.02, 95% CI = 0.98, 1.07).
Conclusions: This study is one of the first to assess workplace victimization among USAR/NG soldiers. Whereas both males and females report workplace victimization in their military jobs, greater victimization was related to drug use for female soldiers, only. Results indicate the importance of developing effective gender-specific prevention and intervention initiatives that address victimization within the unique culture of military service.
Financial Support: Award R01-DA034072 to Gregory G. Homish and the National Center for Advancing Translational Sciences of the National Institutes of Health under award number UL1TR001412 to the University at Buffalo.

M50. Open Board

M51. Assessing Recovery Coach Roles and Responsibilities in Substance Use Recovery

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[1]University of Kentucky, [2]Texas Christian University
Drug Category Other, Any Substance
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Despite growing evidence that peer recovery support services are effective, tools assessing recovery coach roles and responsibilities are limited. The present study presents initial steps used to develop a tool to assess how well recovery coaches fulfill their roles as well as results from preliminary psychometric analyses.
Methods: Items were adapted from the TCU-CEST, an instrument used to measure client functioning and treatment engagement. Additional items were generated to represent recovery coach roles not already captured by the adapted TCU-CEST items. Content validity was reviewed by two outside recovery coaching service delivery experts; further item refinement was based on focus group (n=8) feedback. Revised items (n=61) covering six domains (engagement, satisfaction, rapport, motivation and encouragement, role model, and community linkage) were then administered to 100 males and females with recent peer recovery support utilization. Participants used a 5-point Likert scale to respond to the items. Analysis included descriptive statistics for the sample and items, as well as internal consistency analyses for each domain.
Results: After removing two low performing items, the items for five of the domains had acceptable internal consistency: satisfaction (M = 4.59; alpha = .89), rapport (M = 4.59; alpha = .92), motivation and encouragement (M = 4.70; alpha = .83), role model (M = 4.54; alpha = .91), and community linkage (M = 4.38; alpha = .79). The items for the engagement domain had a slightly lower reliability (M = 4.65; alpha = .68).

Conclusions: Assessing how well recovery coaches are meeting their roles and responsibilities may be important for understanding recovery outcomes. Findings from this preliminary analysis suggest that items cover relevant recovery coach roles and responsibilities, are internally consistent within domains, and can be easily administered to individuals engaging in recovery coaching services. Further refinement of items with other recovery populations is planned.
Financial Support: The study was supported by the University of Kentucky (UG1DA050069) and Texas Christian University (UG1DA050074) research hubs of the NIDA JCOIN cooperative agreement.

M52. Climate Change and Harmful Substance Use – A Risk Pathway Framework

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Drug Category Other, All substance use categories
Topic Other
Abstract Detail Human
Abstract Category Theoretical/Commentary
Aim: Climate change is the most pressing public health challenge facing humanity (World Health Organisation, 2021). More frequent and extreme heatwaves, storms, floods, droughts, and wildfires are causing widespread economic and social disruption and undermining the mental and physical health of global populations. The question of how climate change is affecting patterns of harmful substance use has not been systematically examined, though available evidence suggests negative impacts. The aim of this paper is to describe the scope of the problem and propose an explanatory framework explicating the plausible links between climate change-related stressors and harmful substance use and relapse vulnerability.
Methods (Optional): We review and synthesise climate change and substance use literature to produce a conceptual model that describes the pathways and processes linking climate change to harmful substance use.
Results (Optional): Five plausible pathways link climate change to increasing patterns of harmful substance use: (1) destabilisation of psychosocial, environmental, economic, and geopolitical support systems, (2) increasing rates of mental disorders, (3) increased physical health burden, (4) incremental harmful changes to established behaviour patterns, and (5) worry about the impacts of unchecked climate change. These pathways could operate in isolation, in tandem, or interactively. Young people face disproportionate risks due to their rapidly developing brains and high vulnerability to mental health and substance use problems. We argue that a developmental life course perspective situated within a 'systems thinking' approach can help to conceptualise and track the complex, interacting risks that characterise climate change effects on harmful substance use.
Conclusions: Climate change is driving a confluence of complex, interacting, and ongoing stressors that could increase substance use and relapse vulnerability through multiple independent pathways. Conceptual, methodological, and empirical work is urgently needed to evaluate the magnitude and distribution of the effect of climate change on harmful substance use in order to guide effective preventive and adaptive action.
Financial Support: Francis Vergunst is supported by CIHR and FRQS postdoctoral fellowships.

M53. Examining Factors Associated With "Lack of Readiness to Stop Using" Among U.S. Adults Needing but Not Receiving Substance Use Treatment

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Drug Category Other, Alcohol and other drugs (including marijuana, opioids, sedatives, and stimulants)
Topic Behavior
Abstract Detail Human
Abstract Category Original Research

Aim: A subpopulation of individuals misuse substances and recognize that they may benefit from substance use treatment, however, they are not ready to stop their misuse behaviors; sustaining substance misuse behaviors can increase risk for a substance use disorder (SUD) and/or overdose. A greater understanding of factors influencing these individuals' lack of readiness to stop using may further explain why high-risk populations do not engage in substance use treatment.
Methods: Utilizing 2015-19 data from the National Survey on Drug Use and Health (NSDUH), we conducted multivariate logistic regression to examine factors associated with self-reported "lack of readiness to stop using." Participants (N=1095) were adults aged 18 or older with both a classified and self-perceived need for substance use treatment who did not receive treatment at a specialty facility in the past year.
Results: Roughly 40% of participants were not ready to stop using substances, and 55% self-reported severe psychological distress (Kessler-6 score ≥13). Each additional SUD symptom (OR=1.25, 95% CI=1.13, 1.37) and treatment barrier (OR=1.47, 95% CI= 1.23, 1.77) increased the odds of not being ready to stop using. The odds of not being ready to stop using were also higher for those with a family annual income from $50,000 - $74,999 (OR=2.63, 95% CI=1.26, 5.49) compared to those reporting < $20,000. Conversely, the odds of not being ready to stop using were lower for individuals meeting criteria for illicit drug abuse or dependence only (OR=0.46, 95% CI=0.24, 0.87) (compared to other SUD types) and for those reporting access (OR=0.33, 95% CI=0.20, 0.57), affordability (OR=0.25, 95% CI=0.16, 0.41), and attitudinal barriers toward treatment (OR=0.21, 95% CI=0.11, 0.41) compared to individuals without these same barriers.
Conclusions: These findings signal key characteristics that delineate risk for continued substance misuse behaviors among individuals who recognize that they may benefit from substance use treatment.
Financial Support: This work was supported by the National Institutes of Health (NIH) [Grant No: K02 DA043657 (Dr. Cavazos-Rehg)] and the National Institute on Drug Abuse (NIDA) [Grant No: T32DA015035 (Dr. Cunningham-Williams and Dr. Kathleen Bucholz)].

M54. Lessons Learned From Adapting Screening and Brief Intervention (SBI) to Prevent Substance Use Dependence Among Primary Care Patients in the New Age of Telehealth

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Drug Category Other, ATOD
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: To establish new processes for clinic collaboration and patient engagement during development and piloting of a screening and brief intervention (SBI) before full RCT launch.
Methods: Quit Using Drugs Intervention Trial (QUIT) is an efficacious SBI that reduced drug use among low-income primary care patients with risky drug use. QUIT-Mobile integrates text-message self-monitoring and automated feedback to enhance and sustain drug use reductions for a new hybrid-type 1 effectiveness implementation study. Patients (n=10) were randomized into one of three groups: QUIT, QUIT-Mobile, and usual care. Patients in the QUIT and QUIT-Mobile arms received brief advice from their Primary Care Provider, reinforcing provider video, health education resources, and two telephone health coaching session. The QUIT-Mobile arm also received self-monitoring text-message surveys and automated feedback messages.
Results: Lessons learned included: (1) Ongoing communication and clinic involvement are vital to ensuring an integrated approach and to not disrupt clinic processes; (2) Clinics need make project announcements to all patients with upcoming appointments by mail, social media, or mass text-messages, and post flyers in waiting and exam rooms due to increased patient mistrust of screening text message and phone call outreach; (3) Flexibility is required for recruitment processes and protocol and timeline adaptations when clinics are overwhelmed (i.e., winter surge and flu season); (4) Engage all clinic staff (i.e., front desk staff) so they are aware of study and plan for booster trainings; and (5) Adapting protocol for telehealth can have cost implications.
Conclusions: The uncertainty caused by the COVID-19 pandemic has caused both an increase in Americans using illicit substances as coping mechanisms and caused researchers to explore unchartered territory in adapting in-person protocols for telehealth. If effective, this interventions will be integrated into routine

primary care as part of behavioral health efforts following recommendations of the Affordable Care Act and the Mental Health Parity Act.
Financial Support: This research was supported by National Institute on Drug Abuse (NIDA: R01DA047386).

M55. Principles and Metrics for Evaluating Oregon's Drug Decriminalization Measure: Centering the Voices of People Who Use Drugs

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Drug Category Other, All illicit drugs
Topic Policy
Abstract Detail Human
Abstract Category Theoretical/Commentary
Aim: In 2021, Oregon became the first US State to decriminalize personal possession of small amounts of all drugs while expanding access to addiction recovery and harm reduction services through new investments of $302 million dollars over two years. A departure from decades of punitive approaches to drug problems, Measure 110 (The Drug Addiction Treatment and Recovery Act of 2020) is being carefully followed by policymakers and advocates across the US and around the world. Its success or failure has the potential to shape drug policy in the US for decades to come, but "success" or "failure" is entirely dependent on what outcomes are being measured, how the data are gathered, and whether the findings are understood within the broader context of what is happening on the ground in Oregon. Evaluations of novel drug policies like Measure 110 are critical for informing future policy, yet often lack engagement up front with the people who are the most directly impacted by the policies being studied, despite their having valuable insight into what should be measured and how. As a working group of researchers and service providers, we came together to interview people who use drugs in Oregon to get their input into principles for how to evaluate and what constitutes meaningful metrics for effectively determining the outcomes of Measure 110.
Conclusions: This presentation will describe critical information we learned about the approach needed for a robust evaluation, lay out the broad array of valued metrics which were generated, and provide insight into vital information about the context of Measure 110 implementation that will help researchers and policymakers interpret findings of future evaluations. We hope that this work serves as one model for how to center the voices of those directly impacted in research efforts more broadly prior to evaluating new drug policies.

M56. Telehealth Services for Substance Use Disorders

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Drug Category Other, Substance Use Disorder
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: To better understand the short-term effectiveness of intensive outpatient program (IOP) services for substance use disorder (SUD) delivered virtually and in-person within the context of the COVID-19 pandemic. Despite limited data on the delivery of addiction services via telehealth, the COVID-19 pandemic forced many addiction treatment providers to shift their services to virtual formats, aided by temporary changes to federal, state, and local policies. More rigorous assessment is needed for future applications of virtual delivery for outpatient addiction treatment.
Methods: This 12- month longitudinal study presents findings from adults of both sexes at three months post-discharge (n=1,060) from the Intensive Outpatient Program (IOP) between January 2020 and March 2021 (N= 3,642). There were three treatment settings: in-person, hybrid in-person and virtual, and virtual.
Results: Results of this study demonstrate no significant difference in continuous abstinence ($\chi 2 = 0.42$, $p = .81$), general quality of life ($F(2,826) = 2.06$, $p = .13$), financial security ($F(2,767) = 2.30$, $p = .10$),

psychological well-being (F(2,918) = 0.72, p = .49), and confidence in the ability to stay sober (F(2,941) = 0.21, p = .81). at 3-month follow-up between service delivery settings. Respondents that finished the 3-month survey were less likely to report multiple SUDs (31.7% vs 40.5%; $\chi 2 = 24.58$; $p < .001$), and were less likely to be discharged from care against medical instruction (16.8% vs. 32.6%; $\chi 2 = 62.64$; $p < .001$).
Conclusions: The results of this study suggest that virtual delivery of outpatient SUD treatment is an effective alternative to in-person IOP care. These findings set a strong foundation for further examination of how virtual services can be used most effectively for substance use treatment.
Financial Support: The Addiction Alliance of Georgia

M57. Characterizing Behavioral Addiction Symptoms in Adults Receiving Inpatient Substance Use Disorder Treatment

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Drug Category Other, Both Alcohol and Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The prevalence of behavioral addictions (BA; compulsive engagement in a behavior without the ingestion of a substance, resulting in addiction symptoms) is elevated among people with substance use disorders (SUD), relative to those without an SUD. Although BA are associated with poor outcomes in the general population, they are not routinely assessed in SUD treatment settings. The aim of this study was to examine the prevalence of BA symptoms in a treatment-seeking SUD sample, and to compare those with vs. without BA symptoms on clinical and demographic measures, using t-tests, or chi-square tests where appropriate.
Methods: A screening measure of BA (abbreviated Screener for Substance and Behavioral Addictions) was administered to 144 adults (62.5% male) receiving inpatient detoxification and treatment initiation, primarily for alcohol (75%) or opioid use disorders (17.4%). Participants completed the Brief Addiction Monitor and a questionnaire assessing frequency of 4 symptoms of BA, assessed for 3 behaviors: gambling, video gaming, and sexual activity.
Results: 42.4% of the sample endorsed at least 1 BA symptom during the past year. Among participants reporting any BA symptoms, 62.3% reported that compulsive sexual behavior was the most problematic behavior, followed by 19.7% reporting gaming and 18% gambling. Presence of BA symptoms was not significantly associated with age ($p = .07$), sex ($p = .13$), or primary SUD diagnosis ($p = .34$). However, presence of BA was associated with higher frequency of negative affect and sleep problems, and greater severity of interpersonal conflict, during the 30 days before hospitalization ($p < .05$).
Conclusions: Although preliminary, these results indicate that BA symptoms are common among adults seeking SUD treatment and that presence of such symptoms is associated with more severe psychiatric and interpersonal problems. This underscores the importance of assessing BA symptoms in clinical settings, and suggests that understanding the impact of co-occurring BA should be a priority for future research.
Financial Support: Andrew Peckham was supported by NIDA grant K23 DA041506 during completion of this research.

M58. The Impact of National Drug Policy on the Perceptions of Psychoactive Drugs Among Psychiatrists in the United States

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Drug Category Other, Multiple Psychoactive Drugs
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: We examined whether psychiatrists' perceptions about the harms, abuse potential, or therapeutic benefits of four psychoactive drugs differed as a function of drug scheduling.
Methods: A national quasi-experimental online survey was used. Participants (N=181; Mean age=48.7; Female=35%) were randomized to receive 1-of-4 vignettes, each depicting a depressed patient reporting

relief from depressive symptoms after non-prescribed use of 1-of-4 psychoactive drugs (i.e., psilocybin [Schedule 1; Sched1], Desoxyn [Sched2], ketamine [Sched3], or Xanax [Sched4]). Participants then rated their level of agreement with various statements related to their projected management of this clinical scenario, and then rated the four drugs, alongside alcohol (an unscheduled legal drug for comparison), in terms of their safety, therapeutic, and abuse potential.
Results: There were significant differences as a function of vignette condition in mean likelihood ratings of: warning against engaging in drug use again ($p<.01$), being concerned about developing a new psychiatric problem ($p<.001$), being concerned about increased suicide risk ($p<.01$) and being supportive of further use of this drug as part of the treatment plan ($p<.001$). Overall, non-prescribed use of Desoxyn (Sched2) and Xanax (Sched4) was rated more concerning and less acceptable than non-prescribed use of psilocybin (Sched1) and ketamine (Sched3). Compared to psilocybin (Sched1) and ketamine (Sched3), participants rated Desoxyn (Sched2) and Xanax (Sched4) as less safe ($p<.001$) with less therapeutic potential ($p<.001$) and more abuse potential ($p<.001$). Interestingly, mean ratings of safety and abuse/therapeutic potential of alcohol was equivalent to those of Xanax (Sched4) and Desoxyn (Sched2). All three were rated more harmful than psilocybin (Sched1) and ketamine (Sched3).
Conclusions: These results reveal inconsistencies between psychiatrists' perceptions about potential harms, abuse potential, and therapeutic benefits associated with certain psychoactive drugs and those implied by their legal status. This contrast represents a strong argument for a more coherent and scientifically grounded drug policy.
Financial Support: This study was supported by the Drug Enforcement and Policy Center at the Moritz College of Law, The Ohio State University. AKD, is supported by private philanthropic funding from Tim Ferriss, Matt Mullenweg, Craig Nerenberg, Blake Mycoskie, and the Steven and Alexandra Cohen Foundation. AKD is also supported by the Center for Psychedelic Drug Research and Education, funded by anonymous private donors. The funding sources had no role in the study, data analysis, interpretation, or communication of findings.

M59. A Qualitative Observational Study of Implementing Trauma-Informed Care as a Prevention/Intervention Strategy for Substance Use and Related Problems Among Juvenile Justice Youth

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[1]Texas Christian University
Drug Category Other, Substance use
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Juvenile justice (JJ) youth often have histories of complex trauma and dysfunctional family systems, heightening the risk of substance use (SU). Trauma-informed care (TIC) in JJ agencies provides an opportunity for addressing risk factors of SU among these youth. As part of an ongoing project investigating the effectiveness/implementation of a trauma-informed intervention – Trust-based Relational Intervention® (TBRI®) – among JJ-youth, this study explored staff perceptions of TIC/TBRI as a SU prevention/intervention strategy and factors pertinent to implementation of TIC broadly and TBRI specifically.
Methods: Eighteen focus group interviews were conducted with 92 staff (24 administrators, 23 supervisors, 39 direct care staff, and 6 teachers) from 4 juvenile residential facilities with varying degrees of TIC/TBRI exposure (0-11 years). Thematic analysis, enhanced by firsthand observation and field notes, was used to explore themes emerging from the interviews regarding staff perception, attitudes, and needs/recommendations.
Results: All staff recognized TIC as a prevention/intervention strategy for SU and most reported a need to address secondary trauma-related stress. Staff from the site(s) with no TIC/TBRI exposure expressed needs for generalized training on TIC and targeted training on addressing youth's day-to-day needs with a trauma-informed approach. Staff with some TBRI exposure demonstrated a mix of staff buy-in and resistance to implementing TBRI and expressed a need for more real-life examples of TBRI application. Staff with the most TBRI exposure emphasized the importance of (1) providing frequent TBRI training to the entire workforce and involving families in the trauma-informed treatment plan, (2) more intensive, specialized training on TBRI implementation, and (3) collaborating with other JJ agencies.

Conclusions: The varying degrees of perceptions towards TIC among these facilities reflect the nature of the shift from a corrections-oriented approach to TIC. Specialized implementation plans are needed to help agencies discuss challenges and strategies to enhance the implementation of TIC.
Financial Support: NIDA; Grant 1UH3DA050250, Danica Knight, Principal Investigator

M60. An Intervention to Address the Self-Stigma of Substance Use and Criminal Involvement: Feasibility, Acceptability, and Preliminary Effectiveness

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Drug Category Other, Drug use disorder
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: People in the justice system with addiction experience severe stigma that can impact how they think about themselves (i.e., self-stigma). Self-stigma is associated with distress, poor therapeutic alliance, and other negative social-behavioral outcomes, making it an important treatment target. Although there are effective interventions for reducing self-stigma, none have been examined with justice-involved people. This study aimed to adapt and pilot a self-stigma intervention for justice-involved individuals experiencing addiction, and to determine its feasibility, acceptability, and preliminary effectiveness.
Methods: Acceptance and commitment therapy for substance use self-stigma (Luoma et al., 2008) was adapted to also emphasize criminal record stigma in an open trial with adults diverted to drug court after arrest (n=10). Before and after treatment, participants completed adapted versions of the Self-Stigma of Mental Illness Scale (SSMIS) and Stigma Mechanisms Scale (SMS) to assess internalized stigma of substance use and criminal involvement. T-tests were used to compare pre- and post-test measures. Retention rates and intervention engagement were tracked alongside participant feedback on a satisfaction questionnaire and qualitative interview.
Results: There was a reduction in criminal record internalized stigma on the adapted SSMIS from pre- (M=3.50, SD=.69) to post- (M=2.76, SD=.71) intervention ($t(6)=1.98$, $p= .10$, $d=.75$), as well as the internalized stigma subscale of the adapted SMS from pre- (M=15.14, SD=3.58) to post- (M=14.00, SD=2.16) intervention ($t(6)=1.43$, $p=.20$, $d=.54$). There was a 70% retention at the post-intervention assessment. Qualitative interviews and satisfaction questionnaires (range 1-10, higher scores indicate more positive responses) suggested that participants enjoyed the intervention (M=7.86, SD=.60) and found it helpful (M=8.26, SD=.46).
Conclusions: The adaptation of acceptance and commitment therapy for substance use self-stigma was feasible and acceptable with justice-involved people. Preliminary results are being used to inform an ongoing JCOIN-funded pilot study investigating a multi-level stigma intervention in the justice system.
Financial Support: ETSU Major Research Development Committee grant

M61. Associations Between Automated Session Elements and Gold Standard Ratings of Motivational Interviewing

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Drug Category Other, General SUD psychosocial intervention
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Current gold standard rating systems of Motivational Interviewing (MI) sessions are time and resource intensive. We aimed to identify elements of motivational interviewing sessions that could be automated.
Methods: We transcribed 145 sessions conducted as part of a motivational interviewing training study. These transcripts were coded for 12 data elements hypothesized to be associated with motivational interviewing session quality, including basic session elements (i.e. therapist to client word ratio) and summary variables calculated by Pennebaker's linguistic inquiry and word count (LIWC) system.

Correlations were calculated between these data elements and gold standard MITI ratings indices for motivational interviewing session quality.
Results: After Bonferroni correction, significant correlations existed between the therapist to client word ratio and MITI indices of spirit (r= -0.34, p<.0001), empathy (r=- 0.32, p= .0001), % open questions (r=-0.3, p= .0003), reflection to question ratio (r=-0.34, p<.0001), with higher ratios of therapist words correlating with lower scores and higher therapist speech correlating with greater therapist MI non-adherent behaviors (r=0.26, p=0.0016). The proportion of session turns ending in a question mark was also negatively associated with the reflection to question ratio (r=-0.41, p<.0001). The LIWC analytic score on therapist talk was significantly positively associated with the reflection to question ratio (r= 0.25, p=0.003).
Conclusions: Several automatable session elements are promising as indicators of session quality. Therapist to client speech ratio appears to be most strongly associated with MI session quality and may be a useful element to incorporate into therapist training.
Financial Support: This project was supported by the Smithers Foundation grant #7290. The original MI training study was funded by NIDA 5R01DA016950.

M62. Factors Associated With Recovery Housing Availability for Justice-Involved Individuals in the Community

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Drug Category Other, SUD Recovery
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use and criminal justice involvement are often connected, highlighting the need for recovery support services for justice-involved individuals. Despite a strong evidence base, availability of recovery housing in the US for justice-involved individuals is not well documented. Using data from the National Study of Addiction and Treatment Recovery Residences and US Census, this study examines availability of recovery housing for justice-involved populations.
Methods: Census data were used to identify counties with local jails, state prisons, and/or federal criminal justice facilities. Geospatial analyses characterized county-level recovery housing. Multilevel logistic and negative binomial regressions assessed county-level associations between criminal justice facilities and recovery housing availability and density, adjusting for county-level rurality, proportion of Black residents, proportion of Latino residents, median home value, median rent as proportion of income, proportion of vacant homes, and proportion of units renter-occupied.
Results: Fully adjusted models show that the odds of any housing are 2.37 higher in counties with local jails and 1.76 times higher in counties with state prisons ($p < 0.001$). Similarly, recovery housing density is 2.07 times higher in counties with local jails and 1.57 times higher in counties with state prisons ($p < 0.001$). Federal prisons are not significantly related to odds of any housing or housing density in adjusted models ($p > 0.05$). Models also show significant inverse associations between county rurality and recovery housing (e.g., significantly lower odds of any housing and lower housing density in rural vs. urban counties) when examining only counties with local jails.
Conclusions: Associations between recovery housing and criminal justice facilities highlight a need to ensure linkage to and coordination among recovery housing operators and correctional systems. Rural paucity of recovery housing, especially in counties with local jails, suggests a need for additional recovery residences in these communities in particular.
Financial Support: R01AA027782

M63. Improving Access to High-Value, High-Cost Medicines: The Use of Subscription Models in the United States for Hepatis C Virus Medications

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Drug Category Other, Injection Drugs
Topic Treatment
Abstract Detail Human

Abstract Category Original Research
Aim: Hepatitis C virus (HCV) can be cured with direct-acting antiviral medications, but state Medicaid programs often restrict access to these lifesaving medications owing to their high costs. Subscription-based payment models (SBPMs), wherein states contract with a single manufacturer to supply prescriptions at a reduced price, may offer a solution that increases access. Our objective was to estimate changes in Medicaid-covered HCV prescription fills after Louisiana and Washington implemented SBPMs in 2019.
Methods: We examined trends in prescription fills of Medicaid-covered direct-acting antiviral HCV medications in Louisiana and Washington after implementation of SBPMs. A synthetic control approach was used to compare changes in HCV prescription fills between states that did and did not implement SBPMs. The unit of analysis was state-quarter. Outpatient direct-acting antiviral HCV prescription fills from the Medicaid State Drug Utilization Data files were obtained from all 50 US states and the District of Columbia from 2017-2020.
Results: In the year preceding SBPM implementation, the mean (SD) rate of quarterly HCV prescription fills per 100 000 Medicaid enrollees was 43.1 (8.6) prescriptions in Louisiana and 50.1 (4.1) in Washington. After SBPM implementation, the mean (SD) rate of quarterly HCV prescription fills per 100 000 enrollees was 206.0 (51.2) prescriptions in Louisiana and 53.9 (11.0) in Washington. In synthetic control models, SBPM implementation in Louisiana was associated with an increase of 173.5 (95% CI, 74.3-265.3) quarterly prescription fills per 100 000 Medicaid enrollees during the following year, a relative increase of 534.5% (95% CI, 228.7%-1125.0%). Washington did not experience significant changes in prescription fills following SBPM implementation.
Conclusions: Louisiana experienced substantial increases in HCV medication use among its Medicaid-enrolled population following SBPM implementation, whereas Washington did not. These differences may partially be explained by state-level variation in SBPM implementation, historical restrictions on access to HCV medications, and responses to the COVID-19 pandemic.
Financial Support: Agency for Healthcare Research and Quality (K12 HS026395); National Institute of Drug Abuse (T32-DA041898-03)

M64. Infant Caregiving and Postpartum Substance Use: A Review of the Literature

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Drug Category Other, Multiple substances
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Literature Review
Aim: Infant caregiving practices may protect against postpartum substance use, possibly via the modification of hormones. For instance, breastfeeding, a known protective factor against postpartum substance use, reduces estrogen – a hormone that can promote the use of substances. Although other infant caregiving activities (e.g., skin-to-skin contact) also modify hormones, less is known about how these activities may influence postpartum substance use. Thus, the aim of this literature review was to explore a temporally sensitive link between infant caregiving and postpartum substance use; to possibly provide evidence for the role of hormones as a biological mechanism of action within this relationship.
Methods (Optional): Using a combination of seven infant caregiving (e.g., consoling) and five substance (e.g., cannabis) keywords, we searched PubMed, Embase, and Scopus. We restricted to research on human and published in English since 2000. Additionally, we only included articles that examined the infant caregiving activity in mothers as a predictor of substance use. Two independent reviewers completed a two-stage review of articles to review the title/abstract first, and then the full article. A third reviewer resolved any disagreements.
Results (Optional): Of 413 articles initially identified, 26 were included. Most (n=21) identified a protective effect of breastfeeding on postpartum cigarette smoking. Breastfeeding was also protective against postpartum use of alcohol (n=2), cannabis (n=1), and other drugs (n=1). However, three articles identified a null association between breastfeeding and use of cigarettes (n=2) and alcohol (n=1). A single article identified a protective effect of mother-infant bonding on postpartum cigarette smoking relapse.
Conclusions: In brief, while the literature on this topic is encouraging, it is limited by a heavy focus on breastfeeding and cigarette smoking. Additional research is needed to explore other infant caregiving

activities and other substances, and the possible role of hormones as a biological mechanism within these relationships.
Financial Support: This abstract is supported by NIH/NICHD DP2HD105541.

M65. Transition to Virtual Addiction Treatment After Onset of the COVID-19 Pandemic Among Adults With Drug Use Problems in an Integrated Healthcare System

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Drug Category Other, All substances except alcohol and nicotine
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: To evaluate impacts of the COVID-19 pandemic on addiction treatment utilization, including virtual care, among adults with drug use problems.
Methods: We analyzed electronic health record and claims data from Kaiser Permanente Northern California for two cohorts of adults with drug use problems (disorders or other substance-related diagnoses): pre-COVID (March to December 2019, n=22,160) and post-COVID onset (March to December 2020, n=20,078). Generalized estimating equation models were fit to examine changes in Healthcare Effectiveness Data and Information Set (HEDIS) addiction treatment initiation and engagement, treatment retention and opioid use disorder (OUD) pharmacotherapy from pre- to post-COVID, adjusting for patient characteristics. Virtual treatment initiation and engagement were examined separately. Potential disparities by age and race/ethnicity were examined.
Results: Treatment initiation increased from 30.1% pre-COVID to 33.6% post-COVID [adjusted odds ratio (aOR)=1.18; 95% CI=1.13, 1.24]. Initiation increased among patients 18-49 years (aORs=1.15 to 1.32) but not in older patients (≥50 years). Virtual treatment initiation increased substantially (aOR=4.01, 95% CI=3.74, 4.31), with the greatest increases in patients 18-34 years (aOR=5.48; 95% CI=4.89, 6.14) and Asian/Pacific Islander (aOR=5.72; 95% CI=4.27, 7.66), Black (aOR=4.71; 95% CI=3.74, 5.93), and Latino/Hispanic patients (aOR=4.09; 95% CI=3.49, 4.79). Among patients who initiated treatment, engagement increased from 27.3% to 31.6% post-COVID (aOR=1.22, 95% CI=1.13, 1.33) and retention increased by half a day (95% CI=0.2, 0.8), with no variation by age or race/ethnicity. Among patients who initiated treatment virtually, treatment engagement and retention increased more substantially. Virtual treatment engagement increased most for patients 35-49 years. There were no changes in OUD pharmacotherapy.
Conclusions: In an insured population from a large integrated healthcare system, addiction treatment utilization, especially virtual care, increased after onset of the pandemic. Findings suggest that younger patients and historically minoritized groups benefitted considerably from the transition to virtual care in this healthcare system, with the potential to address treatment gaps.
Financial Support: This study was supported by a supplemental award for a grant from the National Institute on Drug Abuse (UG1DA040314-S3).

M66. "Tired of Lying About Who I Was": A Grounded Theory of Drug Use Disclosure in Research Settings Among Drug Use Researchers

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Drug Category Other, Any illegal drug
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: This study aimed to use grounded theory to construct an explanatory theory to uncover the drug use/nonuse disclosure process among drug researchers. Despite the value of experiential knowledge, drug

use within the drug research community is a heavily stigmatized and hot topic. Few studies have documented drug researchers' drug use and their decision to disclose use/nonuse in professional settings.
Methods: A cross-sectional online survey was distributed via emails to published researchers and social media. Drug researchers from 40 countries provided information on their own drug use and disclosure of use (or lack thereof) in professional settings in a write-in text box. Grounded theory was used to develop the disclosure process and related themes.
Results: The sample (n=656) was 53% women, 74% had a terminal degree, and 80% worked in academia. Most (87%) reported lifetime drug use and 47% reported recent (past 3-months) use. Among 557 researchers who used drugs, 59% disclosed use to colleagues at their home institution, 59% to colleagues outside their home institution, 25% to research participants, 11% in their research/scholarship, and 34% in other public contexts. The disclosure process included identifying as a drug user and considering consequences of disclosure. Themes that emerged included the degree, context, and meaning of drug use disclosure in society and how drug use experience informs research.
Conclusions: Our findings are consistent with previous research dichotomizing the importance of drug use (as best described by a respondent): "He's used drugs-he's biased!" and "He's not a drug user-what would he know!" These data provide an opportunity to reflect upon our positionality as researchers and the impact our own drug use/nonuse may have on the field.
Financial Support: DCO was funded, in part, by the Center for Drug Use and HIV|HCV Research (P30 DA011041).

M67. Barriers to Implementation of Substance Use Disorder Care Within a Local Veteran's Health Administration System

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Drug Category Other, Delivery of SUD Care
Topic Health Services
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Within our local VA system we have identified specific metrics that monitor the delivery of substance use care to veterans, and deficits therein. Substance use treatment services are not routinely available throughout VA Regional Medical Centers. Many facilities do not have a full-time substance abuse staff, and to an extent, the expansive VA network of outpatient primary care providers do not have training or experience in the assessment, treatment, and management of substance use disorders. This creates a gap in care for those who require specialized expertise.
Aims:
1. Identify the VHA strategic analytics for improvement and learning metrics (SAIL) Related to SUD, to demonstrate current veterans engaged in SUD care.
2. Develop implementation methods to improve delivery of SUD Care
Methods (Optional): Quantitatively
- Identify and evaluate SAIL Metrics relating to SUD, and percentage of veteran population meeting set metrics
- Establish the prevalence of substance use diagnoses during inpatient and ER encounters

Qualitatively
- Construct Needs Assessment for SUD CARE
- Assess barriers and facilitators to implementation of an addiction consult service using Implementation Science Framework

Conclusions: After developing methodologies and identifying deficiencies of SUD care delivery to our veteran population, our proposed interventions faced immediate opposition. Our failure to implement and expand SUD services along with institutional barriers beg further critical evaluation and collaborative efforts on local, regional, and national levels within the VHA system. This case outlines an implementation science approach that, if successful, could be applied from the local level to the national level when addressing service delivery deficiencies for veterans with substance use disorder.
Financial Support: RAMS (NIDA R25DA033211)

M68. Availability of HIV, HCV, Substance Use Disorder Treatment and Other Medical Services at U.S. Syringe Service Programs

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Drug Category Other, Injection drug use
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: This study aims to describe medical health services offered on-site at syringe services programs (SSPs) in the U.S. and examine SSP characteristics associated with offering these services.
Methods: We used the national Dave Purchase Memorial survey of SSPs (N=151) to identify and describe the following medical services offered on-site at SSPs in 2019: HIV treatment, HCV treatment, PrEP, medications for opioid use disorder (MOUD), wound care, other primary care (other than wound care), and/or mental health medication treatment. We examine SSP characteristics associated with offering one or more of these services on-site using Chi-square analysis and multivariable logistic regression.
Results: At least one medical service was offered on-site by 65% (n=99) of SSPs with 31 offering one service, 30 two services, 18 three services, and 20 four services or more. The frequency of on-site services offered (in order) was: wound care (73% of SSPs), other primary care (40%), PrEP (36%), mental health (33%), MOUD (32%), HCV treatment (21%), and HIV treatment (16%). Only 42% of SSPs with on-site services had a clinical provider available on site who could prescribe medications, and 56% had a phlebotomist on site. Multivariable analysis found that urban location (ref=rural, aOR=1.27) and having 50% or more of budget from public funding (ref=none, aOR=1.29) were significantly associated (p-value ≤0.05) with offering one or more on-site health services at SSPs.
Conclusions: Most SSPs were offering on-site medical services in 2019 with a wide variety in the type and number of services, but the majority did not have a prescribing clinical provider available. SSPs in rural areas and those with less public funding will benefit from additional support and collaboration to provide on-site medical services. Future research will describe health models employed at SSPs and explore the sustainability and feasibility of implementing these services in different SSP settings.
Financial Support: NIDA support from the following grants: R01DA027379, P30DA040500, and K01DA048172

M69. Syringe Service Program Staff Experiences and Wellbeing During the COVID-19 Pandemic

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Drug Category Other, All
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Syringe service programs (SSPs), which provide a range of harm reduction services to people who use drugs, were deemed essential public health services in the United States early in the COVID-19 pandemic. U.S. SSPs then underwent unprecedented shifts in operational procedures, including closures of physical sites and staff redeployment into pandemic response efforts. Given the magnitude of the pandemic and the critical role of SSPs during this crisis, we sought to examine SSP staff experiences and wellbeing to inform future pandemic preparedness and emergency response efforts.
Methods: From July-October 2020, we conducted semi-structured interviews with SSP staff representing four organizations in diverse regions of Massachusetts. Trained interviewers administered virtual qualitative interviews, which were audio-recorded, transcribed verbatim, and coded using NVivo v12. Thematic analysis identified common occupational experiences and related impacts on wellbeing during the COVID-19 pandemic.

Results: Among 18 participants, 12 (67%) had client-facing roles (as harm reduction specialists, counselors, and outreach workers) and 6 (33%) worked in program coordination, management, and leadership. To meet increased client needs during the pandemic, SSPs rapidly adapted and expanded their services (including food distribution and SARS-CoV-2 testing of clients and surrounding communities), which contributed to staff overexertion. While some narratives revealed SSP staff resilience and protective factors, they were frequently anxious about the risk of occupational exposures to SARS-CoV-2, and simultaneously, concerned about reduced social connection with clients and coworkers due to operational adaptations to accommodate infection prevention (e.g, physical distancing, personal protective equipment).
Conclusions: U.S. SSPs rapidly adapted to help address the COVID-19 pandemic, resulting in operational changes that threatened staff wellbeing. Our findings suggest that during prolonged, complex public health emergencies, enhanced occupational supports should be provided to SSPs to prevent burnout and promote wellness for this essential sector of the public health workforce.
Financial Support: First author was supported by the Medical Student Summer Research Program at Boston University School of Medicine and NIDA grant R25DA013582. Second author was supported by NIDA R25DA033211 and NIAID T32AI052074. Last author was supported by NIH grants K01DA043412, 5K01DA043412-04-S, and R01DA051849.

M70. Determinants of Willingness to Pay for a Drug/Alcohol Problem-Free Day Over Time, Among HIV+ Individuals Who Use Drug/Alcohol in South Africa

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Drug Category Other, Alcohol and substance use
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Over the past decade, drug use has increased around the world, with the highest rates of increase occurring in developing counties. South Africa is one such country, with observed increases in any past 3-month drug use of 3.7% in 2008 to 4.4% in 2012, among persons 15 years old and older. Alcohol is the primary substance misused in South Africa, with 7.5%-31.5% of South Africans having or being at risk of developing an alcohol use disorder. The purpose of this analysis is to estimate the value placed on a day free from drugs/alcohol at several timepoints, by HIV+ individuals who use alcohol/drugs in South Africa, and assess the psychosocial, financial, and environmental factors that influence that value.
Methods: A retrospective secondary analysis of longitudinal data from a randomized clinical trial testing the effectiveness of a primary care based, integrated counseling intervention ("Khanya") to improve SUD and HIV treatment adherence among HIV+ individuals who use drugs in Cape Town, South Africa. Participants' willingness-to-pay for a day free of alcohol/drug use was estimated using the open-ended contingent valuation method. We estimated a multivariable generalized linear model (GLM) regression to examine individual-level determinants of the value placed on a day free of drug use by the study population, after controlling for potential confounders. The primary variable of interest was willingness-to-pay for a day free of drugs/alcohol.
Results: Increase in general health perceptions in the ACTG-SF21 health-related quality of life survey was associated with substantially lower willingness-to-pay for a day free of alcohol/drug use. Other demographic and economic-related variables, by themselves, were not associated with willingness-to-pay for a day free of alcohol/drug use.
Conclusions: Our findings highlight the importance of ensuring individuals with OUD are linked not only to MOUD, but also treatment for their comorbid conditions upon release from incarceration.

M71. Screening in Trauma for Opioid Misuse Prevention (STOMP): Results From a Prospective Cohort of Victims of Traumatic Injury

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Drug Category Opiates/Opioids
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: The current study sought to identify baseline patient and injury-related factors predictive specifically of (1) opioid misuse and (2) the development of opioid use disorder at 6-months following a traumatic injury
Methods: Participants were Trauma and Orthopedic Surgical Services patients at a Level I Trauma Center who were English speaking, aged 18-75, received an opioids prescription at discharge, and were under control of their own medications at the time of discharge. Baseline measures included validated self-report instruments for psychosocial factors, such as anxiety, depression, pain coping, and social support. Health record data included diagnosis codes, procedures, Injury Severity Score, and pain severity (0-10 scale). Opioid use disorder (by Clinical International Diagnostic Interview-Substance Abuse Module) or opioid misuse (individual survey items) were assessed at 24 weeks post-discharge
Results: 295 patients enrolled with 237 completing the 24 week assessments. Stepwise regression modeling demonstrated pre-injury PTSD symptoms, Opioid Risk score, and length of stay predicted misuse and addiction [likelihood of opioid misuse: PCL-5 [OR 1.06, 95%CI (1.02, 1.10)]; Opioid Risk Tool [1.17 (1.04, 1.34)]; length of stay [4.32 (1.24, 17.1)]. The final regression models for opioid misuse and for opioid use disorder had highly favorable areas under the receiver operating curve (0.880 and 0.943 respectively).
Conclusions: Pre-injury presence of PTSD-related symptoms, impaired pain coping, and hospitalization > 6 days predicted opioid misuse and opioid addiction at 6 months after hospital discharge. Behavioral screening and management strategies for anxiety-related syndromes appear warranted in the population of traumatic injury victims to optimize pain management and reduce opioid-related risks.
Financial Support: Wisconsin Partnership Program--Collaborative Health Sciences Award

M72. Similarity of Engagement Across Age Groups of Patients Treated With a Prescription Digital Therapeutic for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Prescription digital therapeutics (PDTs) are software-based treatments evaluated for safety and effectiveness by the FDA. This study evaluated age-related distributions and associations between product use (i.e., engagement) and age, among patients using PDTs for treating opioid use disorder (OUD) along with buprenorphine therapy.
Methods: De-identified data from patients completing at least 1 lesson in a 12-week course of PDT treatment between 1/1/19 and 11/30/21 were obtained from a database of PDT user data. The PDT delivers an OUD-specific form of cognitive behavioral therapy. Descriptive statistics were used to evaluate levels of engagement across the 12-week treatment period as a function of age. Linear and logistic regression was used to evaluate relationships between outcomes and age. Evaluated were: days with any activity in the PDT, lessons completed, and retention in the PDT defined as any activity in weeks 9-12 of treatment.
Results: Meeting evaluation criteria were 5,956 patients, 15% (905) were 18-29 years, 47% (2768) were 30-39, 25% (1503) were 40-49, and 13% (780) were ≥ 50 years. 50% of the sample was female, 34% male, and 16% had unidentified sex. Median active days in the age categories (out of 84 possible days) were: 19, 21, 23, and 20 respectively; median lessons completed (out of 62 possible) were 22, 27, 29, and 26.5 respectively. Percent retained was 68%, 74%, 75%, and 72%. No associations were observed between these outcomes and age (R2 <0.4% for active days and lessons completed; odds ratio/year for retention was 1:01 (95% CI 1.00-1.01).
Conclusions: Similar levels of product use (i.e., engagement) and PDT retention were seen across a wide range of ages in a large sample of adult patients who received a PDT for behavioral treatment of OUD. This PDT appears to have broad acceptability and potential utility to improve outcomes across age groups.
Financial Support: Pear Therapeutics

M73. The Impact of Opioid Agonist Treatment on Hospitalisations for Injecting-Related Diseases: A Retrospective Data Linkage Study

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: To determine the impact of opioid agonist treatment (OAT) on hospitalisations for injecting-related diseases (IRD), and to examine trends in incidence over time.
Methods: We conducted a retrospective state-wide cohort study using linked administrative data. The cohort included 47 163 individuals entering OAT between 1 August 2001 and 31 December 2017 in New South Wales, Australia, with 454 951 person-years (PY) of follow-up information. Outcomes were incident hospitalisations for IRD, including (ICD-10) skin and soft tissue infections, endocarditis, sepsis, osteomyelitis, septic arthritis, venous infections/diseases, and other bacterial diseases, as principal or secondary diagnosis. The primary exposure was OAT status, categorised as either (a) out of OAT; (b) OAT induction (i.e., the first four weeks); or (c) OAT retention (i.e., the remainder of time on treatment). Covariates included year, demographic characteristics, and recent hospitalisations.
Results: Of the 47,163 patients in the cohort, 8349 (17.7%) presented with an IRD hospitalisation in the study period. Compared to time out of treatment, retention on OAT was associated with a reduced risk of IRD (adj rate ratio=0.92;95CI confidence intervals [CI]=0.87-0.97;p=0.03). The age-adjusted incidence rates of hospitalisations increased from 34.8 (95%CI=30.2-40.0) per 1000 person years in 2001 to 54.9 (95%CI=51.3-58.8) per 1000 person years in 2017.
Conclusions: OAT retention is associated with reduced hospitalisations for IRD. Our findings also suggest an increase in these hospitalisations over time that warrants further investigation.
Financial Support: The OATS study is funded by the National Institutes of Health (R01 DA144740 PI: Degenhardt). The National Drug and Alcohol Research Centre is supported by funding from the Australian Government Department of Health under the Drug and Alcohol Program. SC holds a Scientia PhD Scholarship from UNSW, Sydney and an Australian National Health and Medical Research Council (NHMRC) PhD Scholarship. SL holds a Fonds de recherche du Québec – Santé research scholar award. TDB is supported by a Dalhousie University Internal Medicine Research Foundation Fellowship, a Canadian Institutes of Health Research Fellowship (CIHR-FRN no. 171259), and the Research in Addiction Medicine Scholars (RAMS) Program (National Institute on Drug Abuse; no. R25DA033211). DL is funded by the National Institute for Health Research (NIHR; Doctoral Research Fellowship DRF-2018-11-ST2-016. This paper presents independent research. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the UK Department of Health and Social Care. AP is supported by an Australian NHMRC Investigator Fellowship (#1174630). LD is supported by an Australian NHMRC Senior Principal Research Fellowship (#1135991) and a US National Institutes of Health (NIH) National Institute on Drug Abuse grant (R01DA1104470). MH acknowledges funding from National Institute of Health Research (NIHR) Health Protection Research Unit in Behavioural Sciences and Evaluation, NIHR Bristol Biomedical Research Centre at Bristol, NIHR School for Public Health Research, and NIHR EPIToPe. NJ acknowledges funding from the ASCEND program grant.

M74. The Revolving Prison Door for the Newly Released Heroin-Related Offenders in Taiwan: The Role of Community-Based Healthcare

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human

Abstract Category Original Research
Aim: The implementation of community-based treatment and rehabilitation programs for scheduled I and II illegal drugs has been scaled up in Taiwan since 2013. The present study assesses the transition probability from prison to treatment and drug-related arrest/reincarceration and explanatory factors.
Methods: Using the National Corrections Records and the National Police Criminal Records, we identified a cohort of 5520 heroin-involved drug offenders released in 2014. Treatment status of heroin use disorders and health care utilization were ascertained from the Methadone Maintenance Treatment Program (MMT) and National Health Insurance Research Database. Competing risk survival analyses were used for predictors evaluation.
Results: Nearly 50% were in middle adulthood (i.e., 35-44 years old), one third had served time from 1 to 3 years, and one-tenth were HIV-positive. 84% had utilized healthcare services during the first six months and 14.2% were enrolled in the MMT within one year of community reentry; the one-year and three-year reincarceration rates were 6.4% and 26.4%, respectively. Positive predictors for methadone treatment engagement included time served in prison (e.g., 1-3 years, Adjusted Hazard Ratio [aHR] = 6.00; 95 % CI = 4.09-8.79), HIV infection (aHR = 2.02; 95 % CI = 1.70-2.41), and substance use disorder-related healthcare (aHR = 12.91; 95 % CI = 11.04-15.11). Using healthcare services within six months of community reentry may significantly lower the hazard of three-year reincarceration by 31%.
Conclusions: Having access to healthcare and engagement in addiction treatment may serve as a promising approach to reduce recidivism in heroin-involved offenders in Taiwan.
Financial Support: This study was supported by the Ministry of Health and Welfare, Taiwan.

M75. Transition of Patients Established on Long-Term Transmucosal Buprenorphine Atreatment to Monthly Buprenorphine Injection

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Buprenorphine extended-release injection (Sublocade®) is indicated for treatment of moderate/severe opioid use disorder in patients who have initiated transmucosal buprenorphine treatment for at least 7 days. Sublocade recommended dosing regimen consists of 2 initial doses of 300 mg monthly followed by maintenance doses of 100 mg monthly. The aim of this analysis was to guide, based on pharmacokinetic simulations, the transition of patients with long-term clinical stability on transmucosal buprenorphine to Sublocade and to assess the need for 300-mg starting doses in this population.
Methods: Simulations were conducted using validated population pharmacokinetic models developed for Sublocade (19 686 observations, 570 subjects) and transmucosal buprenorphine (2826 observations, 204 subjects). Various transition scenarios were assessed, evaluating a series of transmucosal buprenorphine doses from 8 to 24 mg/day and Sublocade starting doses of 300-300 mg, 300-100 mg or 100-100 mg (monthly injections 1-2) followed by maintenance doses of 100 or 300 mg monthly.
Results: Results indicate that patients stable on 20-24 mg/day transmucosal buprenorphine would require two initial doses of 300 mg. In patients stable on 8-18 mg/day, one initial dose of 300 mg would be sufficient, and the second 100-mg injection would maintain the levels of the first injection. Starting Sublocade treatment with 100 mg as the first injection is not appropriate as buprenorphine plasma concentrations would be too low. At steady-state, buprenorphine plasma concentrations achieved with the 100-mg maintenance dose were contained within the range obtained with transmucosal buprenorphine doses of 8-24 mg/day; peak concentrations with Sublocade were generally lower, while trough concentrations were higher to sustain target levels of 2-3 ng/mL.
Conclusions: These analyses provide guidance to physicians for transitioning patients stable on transmucosal buprenorphine to Sublocade and demonstrate the importance of initiating Sublocade treatment with one or 2 monthly doses of 300 mg.
Financial Support: Indivior, Inc.

M76. Factors Driving Treatment Retention Among People With Opioid Use Disorder and HIV in Vietnam: A Qualitative Study

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Integrating buprenorphine treatment of opioid use disorder (OUD) into HIV care can improve care quality and access but may have lower retention than methadone treatment. We investigated patient perspectives into drivers of buprenorphine versus methadone retention among people seeking care for HIV and OUD in Vietnam.
Methods: We conducted face-to-face qualitative interviews with people living with HIV and OUD (n=26) after enrolled in the BRAVO trial comparing HIV clinic-based buprenorphine (n=12) versus HIV clinic care with methadone referral (n=14) in four HIV clinics in Vietnam. Vietnam treatment guidelines required directly observed dosing for both medications. Interviews were professionally transcribed and analysed using thematic analysis with a semantic perspective comparing perspective of those retained and not retained on buprenorphine and methadone at 12 months.
Results: Shared barriers to retention included the requirement of clinic attendance multiple times a week (conflicting with family and employment responsibilities) and physical toll from treatment (sleep disturbance, tiredness, decreased libido, decreased fertility). Shared facilitators of retention included family support (from improved family relationships) and convenience of co-located care when available (saving time by not having to go to two locations). Unique buprenorphine retention barriers included challenges of integrated care (longer lines, participant concern about their HIV status being revealed to broader patient population, time required for directly observed dosing, HIV treatment staff being unfamiliar with OUD). A unique buprenorphine retention facilitator was that patients reported not feeling the sedative effect of opioids while taking buprenorphine. Unique methadone retention facilitators were patients' fear of withdrawal symptoms if required to taper and subsequently having to spend money on opioids.
Conclusions: Study findings suggest that structural factors such as directly observed dosing requirements and confidentiality concerns about HIV disclosure may impede retention in an HIV clinic-based buprenorphine treatment model in Vietnam. Both structural and patient-directed interventions may improve retention in OUD treatment.
Financial Support: National Institute on Drug Abuse (R01DA037441)

M77. A Novel Toll-Receptor 7/8 Adjuvant Increases the Immunogenicity of an Anti-Fentanyl Vaccine and Its Efficacy at Attenuating the Reinforcing Effects of Fentanyl in Rats

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Opioid use disorder and overdose is a major public health problem. Anti-opioid vaccines have shown promise in preclinical studies as a means to reduce the addiction- and overdose- related effects of opioids, but their efficacy has been limited. The purpose of the present study was to determine whether a novel toll-like receptor agonist, INI-4001, can enhance the immunogenicity of an anti-fentanyl vaccine and its efficacy in reducing intravenous fentanyl self-administration (FSA) in rats.
Methods: Male and female rats (n=11-16 per group) were initially trained to self-administer a unit dose of 2.5 µg/kg fentanyl during daily 2-hr sessions. After stable intake was achieved, rats were vaccinated every two weeks with F1-CRM+INI-4001, F1-CRM as a positive control, or CRM (carrier protein alone) as a negative control, while continuing FSA sessions. After completing the initial vaccination regimen (4 vaccinations), the FSA unit dose was varied to obtain a fentanyl dose-response curve as vaccinations continued.

Results: Antibody titers were significantly higher in rats given F1-CRM+INI-4001compared to F1-CRM. Both vaccines increased FSA compared to baseline during the initial 4 vaccinations, while CRM control rats showed no such change. However, the magnitude of the increase was larger in the F1-CRM+INI-4001 group compared to the F1-CRM group. In addition, while both F1-CRM+INI-4001 and F1-CRM shifted the FSA dose-response curve to the right relative to CRM, the shift was greater in rats treated with F1-CRM+INI-4001.
Conclusions: These findings demonstrate that an anti-fentanyl vaccine can attenuate the reinforcing effects of fentanyl. Moreover, the TLR 7/8 adjuvant INI-4001 enhances vaccine immunogenicity. Efficacy in this model is also enhance by producing a greater reduction in the potency of fentanyl. Use of TLR 7/8 adjuvants in vaccine formulations may help maximize the clinical efficacy of vaccines for treating opioid use disorder and preventing overdose.
Financial Support: Supported by NIH/NIAID contract HHSN272201800048C (Evans, PI)

M78. A Statewide Evaluation of the Implementation and Effectiveness of Medications for Opioid Use Disorder in Vermont Correctional Facilities and the Impact of COVID-19

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Individuals with opioid use disorder (OUD) are overrepresented in US correctional facilities. Medications for OUD (MOUD) are the only empirically-based treatments for OUD but not available in most correctional facilities. In 2018, Vermont passed Act 176 to become the second state to offer all three MOUDs to all incarcerated individuals. Subsequently, a state of emergency was declared in March 2020 in response to COVID-19. We aimed to evaluate the implementation and effectiveness of MOUD and the impact of COVID-19 on individuals incarcerated in Vermont.
Methods: This evaluation linked Vermont Department of Corrections (DOC) and Medicaid claims data from 07/01/2017 to 03/31/2021 to assess the implementation and effectiveness of MOUD in the VT DOC and the impact of COVID-19. We describe and compare the time-periods A) before MOUD implementation and before COVID-19; B) after MOUD implementation but before COVID-19; and C) after MOUD implementation and during COVID-19 using chi-square and multi-level logistic regressions.
Results: The proportion of incarcerated individuals who were prescribed MOUD in Vermont increased substantially after Act 176 (0.8% to 33.9%; OR=67.4, 95% CI=49.0, 92.9) and subsequently decreased with the onset of COVID-19 (26.6%; OR=0.7, 95% CI=0.6, 0.8). Most individuals newly initiated MOUD upon incarceration (63.1% before and 53.9% during COVID-19) and most MOUD prescriptions were for buprenorphine (82.6% before and 84.0% during COVID-19). Before Act 176, 33.9% received an MOUD prescription in the community within 30 days after release. This increased to 41.0% after Act 176 (OR=1.4, 95% CI=1.3, 1.7) and then reduced to 35.6% during COVID-19 (OR=0.8, 95% CI=0.6, 0.9). Opioid-related overdoses post incarceration decreased from before (non-fatal=1.2%; fatal=1.1%) to after (non-fatal=0.8%; fatal=<0.03%) Act 176.
Conclusions: Findings demonstrate increased healthcare access associated with MOUD implementation in Vermont correctional facilities as well as a need to improve continuation of care after release in the context of the ongoing COVID-19 pandemic.
Financial Support: NIH HEAL JCOIN Rapid Innovation Grant (1U2CDA050097); National Institute of General Medical Sciences (5P20GM103644-07)

M79. Analyzing Quality of Life Measures Collected in People With Opioid Use Disorder From the NIDA Data Share Initiative: The Implications for Cost-Effectiveness Evidence in Resource Allocation Decisions

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: Research has shown that health-related quality of life (HRQoL) evidence needed to inform models for economic evaluation is limited in the context of opioid use disorder (OUD). This study aims to address this deficiency by analyzing data from the NIDA Data Share initiative to produce results that provide an appropriate representation of the health burden associated with health states typically found in OUD models.
Methods: Trial data were obtained if the following measures were collected: generic measures of HRQoL (EQ-5D-3L, SF-12 Versions 1 or 2) and self-reported opioid use with the Addiction Severity Index. External evidence was used to equate different measures of HRQoL onto the same scale using psychometric methods. A regression analysis was then performed to quantify the HRQoL effects associated with the following variables: non-medicated opioid use (NMOU), injection drug use, treatment with OUD medications, and infectious disease comorbidities. Additional variables, including withdrawal symptoms, were included to account for potential confounders.
Results: Data from six trials were combined producing a sample of 1,964 individuals. In the base case analysis, the following variables were associated with significant (p-value<0.05) reductions in HRQoL values: daily NMOD (vs. no use in the past 30 days), injecting as the main route of administration, HIV positive diagnosis, advanced HIV diagnosis, any other type of substance use. However, when the analysis controlled for self-reported withdrawal symptoms, daily NMOU and injection drug use were no longer significant, suggesting the negative effect of opioid use on HRQoL is driven by the experience of withdrawal.
Conclusions: Results reveal that withdrawal symptoms are a fundamental driver of HRQoL in people with OUD, which are not currently accounted for in existing models. This finding indicates current models may be misrepresenting the lived experience of OUD and, ultimately, may be at risk of yielding suboptimal policy recommendations.
Financial Support: T32 Training Grant (T32 DA023356) and a NIDA Avenir Grant (DP2DA049295)

M80. Assessing Changes in Cognitive Functioning in Individuals With Opioid Use Disorder Enrolled in a Residential Treatment Program

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: To evaluate objective and subjective changes in the cognitive functioning of individuals with opioid use disorder (OUD) who are enrolled in a 28-day residential treatment program (RTP) for substance use disorder.
Methods: Enrolled participants (n=6) had a diagnosis of, and prescribed medication for, OUD. Following admission to the RTP, participants were administered the National Institutes of Health Toolbox Cognition Battery (NIHTB-CB) on two occasions; evaluations were separated by 14.8±2.7 days. Participants also completed the self-report Cognitive Function short-form of the Quality of Life in Neurological Disorder (Neuro-QoL) assessment at the same time points. Paired sample t-tests were utilized to determine within-subject changes over time with the NIHTB-CB Total Cognition Composite, Crystalized Composite, and Fluid Composite uncorrected standard scores (normative mean ± standard deviation (M±SD): 100±15) as well as the Neuro-QoL – Cognitive Function scaled score (normative M±SD: 50±10).
Results: Participants (4 male, 2 female) were 32.0±4.4 years of age with 11.3±2.3 years of education. In addition to opioids, reported co-occurring substance use included methamphetamine (n=3), benzodiazepines (n=2), alcohol (n=2), and cannabis (n=1). During the follow-up assessment conducted approximately 2 weeks following the initial assessment, improvements were noted in NIHTB performances including the Total Cognition Composite ($t(5) = -3.6$, $p = 0.008$), Crystalized Composite ($t(5) = -2.8$, $p = 0.019$), and Fluid Composite scores ($t(5) = -2.8$, $p = 0.020$). Self-reported improvements were also noted on the Cognition Function Neuro-QoL ($t(5) = -2.6$, $p = 0.024$) during the follow-up relative to the initial assessment.

Conclusions: These findings indicate that, in individuals with OUD who are enrolled in a RTP, improvements in objectively measured and self-reported cognitive functioning are apparent throughout the course of treatment. Presented findings will include a larger cohort of participants along with preliminary data exploring potential factors (e.g. premorbid IQ, co-occurring substance use, years of substance use) impacting initial cognitive recovery.

M81. Barriers and Facilitators to No-Cost Pharmaceutical Alternatives to Illicit Drugs During Intersecting COVID-19 and Overdose Health Emergencies in British Columbia, Canada: A Qualitative Study

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To examine barriers and facilitators to no-cost prescription opioids (hydromorphone) and stimulants (dextroamphetamine, methylphenidate) made available under risk mitigation guidelines released in British Columbia (BC), Canada as a harm reduction measure to address an overdose crisis driven by fentanyl and adulterated drugs during the COVID-19 pandemic.
Methods: Since February 2021, qualitative interviews have been conducted with 42 people who use drugs from across BC who reported accessing or attempting to access prescription opioids or stimulants under the risk mitigation guidelines. Interview transcripts were analyzed using inductive and deductive approaches.
Results: While some participants initially accessed prescription opioids or stimulants as an emergency measure to isolate following a COVID-19 exposure or diagnosis, most had accessed – or attempted to access – prescription drugs through primary care practitioners or addiction medicine specialists to limit their exposure to illicit drugs and, in some cases, facilitate social distancing. Participants in urban settings, which had more willing prescribers, reported greater access to prescription opioids and stimulants than those in rural and remote settings characterized by poorer care access and anti-drug stigma. Participants emphasized that program requirements such as daily pharmacy pickup were burdensome and often led to interruptions in access to prescription opioids and stimulants due to competing demands (e.g., housing needs, work schedules) and, in turn, resulted in illicit drug use. Such requirements were particularly burdensome for participants in rural and remote settings due to geographic distance to pharmacies and unreliable access to transportation.
Conclusions: Findings demonstrate how prescriber willingness, geography, and stigma are critical were critical in shaping access to no-cost pharmaceutical alternatives to illicit drugs during the COVID-19 pandemic. Attention to geographic inequities, including through prescriber eduction and other supports, is urgently needed. Meanwhile, low-threshold approaches (e.g., take-home dosing) will likely needed to optimize access.
Financial Support: National Institutes on Drug Abuse (R01DA044181); Canadian Institutes of Health

M82. Buprenorphine Adherence and Its Association With Illicit Opioid Use

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: To describe patterns of daily buprenorphine adherence and assess association between level of adherence and illicit opioid use.
Methods: We conducted a secondary analysis of a randomized controlled trial evaluating a mobile Health intervention for adults with opioid use disorder (OUD) who recently initiated buprenorphine treatment. Weekly study visits over 13 weeks included a urine drug test (UDT) and self-report of daily buprenorphine adherence using the Timeline Followback method. We performed log-linear regression models that

accounted for clustering by participant to assess the associations between UDT negative for illicit opioids and three separate variable definitions of past- week daily adherence: 1) Full adherence (no vs. yes); 2) Low adherence (0-3 days), intermediate adherence (4-6 days) and full adherence (7 days), and 3) a continuous variable of 0-7 days adherent.
Results: Of the 78 participants, only 4 were fully adherent at all visits. Of total visits, 70% had full adherence, 18% intermediate, and 12% low adherence. When compared to less than full adherence, full adherence was significantly associated with UDT negative for illicit opioids (RR= 1.41; 95% CI:1.15-1.72; p=0.001). Compared to low adherence, full adherence (7 days) was significantly associated with weekly UDT being negative for opioids (RR=1.63; 95% CI: 1.22-2.18, p=0.001), while intermediate was not significantly associated (RR=1.27; 95% CI 0.95-1.69, p=0.11). The rate of negative UDT for opioids increases by 7% for each additional day of adherence (RR=1.07; 95% CI: 1.03-1.12, p=0.002).
Conclusions: In this study of patients who had recently initiated buprenorphine, participants did not take buprenorphine as prescribed on nearly one third of reported days. Daily adherence to buprenorphine was significantly associated with having a UDT negative for opioids. Results suggests the importance of buprenorphine adherence to achieve ideal OUD treatment outcomes.
Financial Support: NIH/NIDA (R44DA044053; PI: Seiguer/Tsui)

M83. Clinically Significant Loneliness Among Individuals With Opioid Use Disorders

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Loneliness—a subjective emotional state characterized by the perception of social isolation—is a psychosocial stressor that is associated with increased mortality, opioid use, and is associated with precipitants of relapse among individuals with opioid use disorders (OUD). The purpose of the study was to examine baseline characteristics of a clinical trial testing an intervention to address clinically significant loneliness among individuals with OUD.
Methods: Participants (n = 32) with at least an active moderate opioid use disorder and clinically significant loneliness were recruited using social media advertising. Participants completed a baseline assessment containing measures assessing loneliness (UCLA Loneliness), quality and quantity of social interactions (Duke Social Support Index), substance use and its consequences (TLFB; InDUC), craving (Penn Alcohol Craving Scale), pain and physical functioning, depression, anxiety (PROMIS), and demographics.
Results: To date, the sample is comprised of individuals who are mostly White/Caucasian (78%) and female (63%) with a mean age of 54 (SD=9.7). Depression (M=12.1, SD=3.5) and anxiety symptoms (M=12.2, SD = 4.5) were elevated. Scores on loneliness (M=53.9, SD=9.7) and social interaction measures suggest impaired social functioning. Participants endorsed an average of 8 OUD symptoms representing a severe OUD sample. The sample experienced a high level of opioid craving (M=20.5, SD=7.5) and endorsed numerous overdose risk behaviors.
Conclusions: Individuals with opioid use disorders reporting clinically significant loneliness appear to have a severe clinical profile across interpersonal, substance use, mental health symptoms, and overall functioning.
Financial Support: National Institute of Drug Abuse

M84. Early-Onset Prescription Opioid Misuse in Indiana Youth

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research

Aim: Approximately 10% of youth between the ages of 12-17 report past year prescription opioid misuse (POM) in the United States. POM among adolescents is associated with negative health outcomes and risk behaviors. The current study examined both the prevalence of POM among diverse groups of adolescents and the influence of other substance use, specifically alcohol and cigarette use, in the prediction of early POM use.
Methods: Data came from the cross-sectional state-based 2018 Indiana Youth Survey of students from grades 6-12, ranging in age from 10-17 years (n=93,955). Lifetime use of non-prescribed prescription drugs, alcohol, and cigarettes were assessed by self-report, including ages at first use. A series of analyses were conducted separately for non-Hispanic Black (NHB), non-Hispanic White (NHW), and Hispanic students. First, we estimated the prevalence of POM. Then, using the Kaplan-Meier method, we calculated age of first POM. Next, we estimated Cox proportional hazards regression models to predict age at first POM from ages at first use of alcohol and cigarettes.
Results: Three-percent of non-Hispanic Black, 4% of non-Hispanic White, and 5% of Hispanic students reported POM, with median ages at first use between 13-14 years. Across racial/ethnic groups, onset of drinking was highly predictive of first POM (NHB HR [95% CI] = 13.42 [9.05-19.89], NHW HR [95% CI] = 17.58 [15.82-19.55], Hispanic HR [95% CI] = 12.83 [10.12-16.2], as was onset of cigarette use (NHB HR [95% CI] = 8.10 [5.42-12.10], NHW HR [95% CI] = 14.18 [12.90-15.60], Hispanic HR [95% CI] = 10.22 [8.27-12.64]).
Conclusions: Onset of alcohol and cigarette use were predictive of POM among Indiana youth, suggesting that intervention aimed at preventing early drinking and smoking may also reduce POM among youth.
Financial Support: Indiana University start-up funds (MAP)

M85. First in Human Trial of the Non-Opioid Selective Orexin-1 Antagonist INDV-2000 in Healthy Volunteers

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Drug Category Opiates/Opioids
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: INDV-2000 (C4X3256) is an oral, highly potent, selective Orexin-1 receptor (OX1R) antagonist under investigation for treatment of substance use disorders. In nonclinical self-administration and cue- and stress-induced reinstatement studies, antagonism of the OX1R has been associated with reduction or blockade of drug-seeking behavior. Preclinically, INDV-2000 demonstrated up to 1000-fold selectivity over Orexin-2 receptor (OX2R) activity in human functional cell assays, and sustained brain target engagement with prolonged duration of action. It reduced nicotine self-administration, cue-induced nicotine-seeking behavior and cue-induced reinstatement of cocaine-seeking in animal models.
Methods: This was a single center, phase 1, randomized, double blind, placebo-controlled single ascending dose study to assess safety, tolerability, and pharmacokinetics (PK) of INDV-2000 in healthy volunteers. Assessments included electrocardiograms, laboratory testing, and sedation visual analog scales for 5 days in-clinic, and one out-patient visit 7 days later. Blood PK sampling occurred for 72 hours post-dose. (NCT04413552).
Results: Sixty-four (50 male, 14 female) healthy volunteers (20-55yrs, BMI 18-32mg/m2) participated in 8 ascending dose cohorts between 1 and 720mg. All doses were well tolerated with no treatment emergent adverse events of clinical concern or changes from baseline in laboratory evaluations, electrocardiograms, vital signs, or on physical examination. Additionally, there was limited evidence of OX2R mediated sedation. Across the dose range of 20-720mg, the median time to maximum concentration was 2.0-3.5hrs with mean elimination half-life in the 2.6-5.3hrs range. Exposure increased proportionally with dose in terms of area under the curve and less than proportionally for maximum concentration.
Conclusions: INDV-2000 is a well-tolerated, well-absorbed, highly selective OX1R antagonist in healthy volunteers after single doses up to 720mg. The pharmacokinetic profile showed dose proportional increases in overall exposure up to 720mg.
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M86. How Has Ecological Momentary Assessment Been Used With People Who Are in Medication-Based Treatment for Opioid Use Disorder?

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Literature Review
Aim: This methodologic systematic review aims to 1) synthesize the literature describing Ecological Momentary Assessment (EMA) use among people receiving medication for opioid use disorder (MOUD) and 2) better understand the feasibility and acceptability of EMA use among people receiving MOUD.
Methods (Optional): The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology was utilized. Without date restriction, we searched three library databases (PubMed, CINAHL, Psych Info). We included English, peer-reviewed articles that: a) were intervention or observational studies of people receiving MOUD and b) used EMA. Articles were coded for demographics and EMA structural and procedural characteristics.
Results (Optional): Out of 211 citations, 27 studies with 35 analyses were included. Sample sizes ranged from 5 to 309. Study designs included randomized controlled trials (n=4) and observational studies (n=31) in the background of MOUD treatment. Participants were primarily African American (41-75%) males (55-94%), in all but two studies. Results indicated that adherence to EMA prompts over long periods of time (between 2-28 weeks) during MOUD is feasible. When reported, adherence to EMA prompts was adequate (77-80%). Craving, stress, and mood were the most frequent EMA measures investigated for their relationship to drug use and MOUD treatment outcomes.
Conclusions: Women and pregnant people were underrepresented in all but two studies. As EMA is a promising measurement tool, and a potential intervention component, it is important to test its use in diverse populations, including women and pregnant people. This review demonstrates that EMA is an effective measurement tool to assess momentary states during MOUD. Therefore, researchers could improve ecological validity by adopting EMA methods where self-report recall scales are currently being used.

M87. Improving Linkage and Ongoing Engagement With Outpatient Treatment in Patients Initiating Medication for Opioid Use Disorder While Hospitalized at an Urban Safety Net Hospital: Results From Project HOUDINI LINK

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Project HOUDINI LINK (Hospital Opioid Use Disorder treatment INItiation and LINKage to care) offered 6 months of patient navigation with attendance and abstinence incentives (max $325) to 150 patients initiating medications for OUD (MOUD) at an urban safety net hospital in San Francisco. We compared 30-day post-hospitalization linkage rates to historical controls and investigated predictors of ongoing MOUD treatment engagement at 3 and 6 months.
Methods: Participants began methadone (N=83, 55%), buprenorphine (N=64, 43%) or extended-release naltrexone (XR-NTX; N=3, 2%) during inpatient or emergency department admissions between March 2018 and June 2021 and were referred to outpatient MOUD providers. Univariate and bivariate analyses (SPSS) were used to examine differences in linkage and ongoing MOUD engagement.

Results: Participants were on average 44 years, 71% male, 51% non-white, and 19% Hispanic. Most (76%) were homeless, current smokers (76%), primarily using heroin (69%) or fentanyl (28%), and other substances (stimulants 66%, cannabis 53%, alcohol 32%, benzodiazepines 22%). By discharge, patients were on moderate doses of methadone (M=48 mg) or buprenorphine (M=14 mg) or had received one dose of XR-NTX. Overall, 64% were linked to outpatient MOUD providers compared to 28% of historical controls (OR 4.6, $p<0.0001$). There were no differences in linkage between patients on methadone versus buprenorphine ($p=0.09$) nor ED versus inpatient referral ($p=0.88$). Linkage was significantly associated with housing ($\chi2 =5.64$, $p=0.02$) and recently injecting ($\chi2 =3.9$, $p=0.05$). MOUD engagement was 40% and 30% at 3 and 6 months. Three-month engagement differed by a participant's 30-day linkage ($\chi2=21.45$, $p<0.001$), and housing ($\chi2=5.77$, $p=0.02$), and smoking status ($\chi2 =7.94$, $p=0.005$). 2/3 of participants on MOUD at 3 months were retained at 6 months.
Conclusions: Patient navigation and financial incentives improved linkage rates to outpatient MOUD treatment by 460% compared to historical control in hospitalized patients with high rates of homelessness and co-occurring substance use.
Financial Support: Activities were funded by grants from SAMHSA (6H79TI081419; PI: Tompkins) and NIDA (T32DA007250; mPI Sorensen / Satre).

M88. Initial Safety and Feasibility of Rapid-Induction Buprenorphine Extended-Release Following Opioid Overdose

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid-related overdoses have significantly increased during the COVID-19 pandemic in the United States. Emergency department (ED)-initiated buprenorphine treatment may prevent repeat overdoses and death. This project evaluated the initial safety and feasibility of rapid induction onto extended-release buprenorphine (BUP-XR) within 7-days of presentation to the ED with an unintentional, opioid-related overdose.
Methods: N=19 patients received sublingual (SL) buprenorphine/naloxone (BUP-NLX; 8:4mg) and after 30 minutes, a subcutaneous (SC) injection of extended-release buprenorphine (BUP-XR; 300mg). The initial administration of study medications occurred in either the ED, the inpatient unit, or the affiliated outpatient treatment clinic. Baseline measures included patient demographic characteristics (e.g., age, sex, race/ethnicity, etc.). Primary outcomes for this project included mean Clinical Opioid Withdrawal Scale (COWS) score and prevalence of AEs at the three timepoints. Electronic health data on patient characteristics associated with ED-initiated treatment will be also be presented at the June 2022 meeting as a measure of feasibility.
Results: The majority of patients were Male (89%), Black (95%), and were 46.4 ± 12.1 years of age. The total mean COWS scores decreased sharply from pre-BUP-NLX (5.7 ± 4.8) to post-BUP-NLX (1.9 ± 1.6) and to post-BUP-XR dose (1.4 ± 1.2). One AE was reported pre-BUP-NLX dose and was unrelated to the study. Two AEs were reported after administration of BUP-XR, both of which were mild and related to the BUP-XR.
Conclusions: Overall, we demonstrated initial safety and feasibility of rapid induction BUP-XR among a small sample of adults following an opioid overdose. We did not observe any evidence of precipitated withdrawal or serious adverse events with administration of BUP-XR. Future studies are needed to further examine the feasibility and long-term effects of BUP-XR in a larger, generalizable sample of patients presenting to the ED with unintentional opioid-related overdose.
Financial Support: NIDA T32 DA7027-44, UL1TR002649, U54DA038999

M89. Injection Partnership Characteristics and Hepatitis C Status Associations With Syringe and Equipment Sharing Among People Who Inject Drugs

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: We examined dyadic predictors of syringe and other injection equipment sharing between young people who inject drugs (PWID) and their injection partners, including self and partner HCV status.
Methods: Young (18-30) PWID were recruited for a longitudinal study of social networks and HCV. Primary participants (egos) completed baseline interviews that included reporting on characteristics of injection partners (alters), their relationship, and HCV status. We tested the associations between ego and alter characteristics and syringe and equipment sharing in mixed effects logistic regression analyses.
Results: The sample included 276 individuals with 929 injection partners. Forty-four percent of participants reported sharing a syringe with at least one injection partner. Twenty-five percent reported a positive HCV status, while 34% were unknown. Twenty-two percent of alters were reported as positive and 24% as unknown. Syringe and equipment sharing were associated with younger age, mixed-gender dyads, living in the same household, daily contact, trust, condomless sex, and personal support. In the adjusted model, participants who reported a positive HCV test were more likely to share syringes with an injection partner who was also HCV positive (vs. negative, OR=11.68, 95% CI 1.51-90.49; vs. unknown, OR=20.13, 95% CI 1.55-261.30). For equipment sharing, there were significant main effects for both ego HCV positive status (vs. negative, OR=6.06, 95% CI 1.88-19.56) and alter HCV positive status (vs. negative, OR=3.29, 95% CI 1.29-8.39). Trust and condomless sex had independent associations with syringe and equipment sharing, and sharing a residence was independently associated with equipment sharing.
Conclusions: Young PWID who have tested positive for HCV tend to share syringes with other PWID who are likewise positive. Similar serosorting was not found among PWID with a recent negative result or unknown status. PWID who may have cleared a HCV infection risk re-infection by sharing injection equipment with HCV-positive injection partners.
Financial Support: This work was supported by a grant from the National Institute on Drug Abuse [grant number R01DA043484].

M90. Is Naloxone Distribution Risky? Attitudes About Naloxone Distribution at the Start of Medical School and Two Years Later

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Each day, 133 people die from opioid overdose. These deaths are fully preventable by using the opioid antagonist naloxone; however, significant barriers to naloxone access remain. Many healthcare workers are unaware of laws and guidelines regarding naloxone distribution and may contribute to stigma and misinformation surrounding its use. In this study, we evaluated medical student knowledge and attitudes towards naloxone distribution across two years of training.
Methods: Medical students in the Class of 2023 (N=167) completed surveys upon entering their first and third years (M1 and M3). Surveys included the Naloxone-Related Risk Compensation Beliefs (NaRRC-B) scale and additional questions regarding risks and benefits of naloxone distribution. Outcomes were explored using descriptive statistics and used repeated measures ANOVAs to evaluate changes in outcomes between M1 and M3.
Results: Upon entering medical school, 49.1% believed that naloxone should be available to everyone without a prescription, 12.6% thought it should not, whereas the remaining 38.3% were unsure. The major reasons students did not support naloxone distribution were concerns about: 1) side effects, 2) condoning substance use, 3) increasing substance use. Attitudes significantly changed by the start of M3, with 85% of students agreeing that naloxone should be available to everyone prescription-free, and only 3.6% disagreeing.

Conclusions: Medical students must be prepared to support individuals at risk of opioid overdose; this requires them to have an accurate, non-stigmatizing understanding of the risks and benefits of naloxone distribution. We demonstrate that pre-clinical training provides some education on this topic; however, further work is necessary and detailed harm reduction training is needed within medical education. Future studies should explore how this knowledge changes over clinical training and how differences in knowledge and attitudes impact clinical behavior.
Financial Support: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Trainee effort was supported by the National Institute on Drug Abuse of the National Institutes of Health under award number F30DA052118 (TEHM).

M91. Lack of Effect of Different Pain-Related Manipulations on Opioid Self-Administration, Reinstatement of Opioid Seeking, and Opioid Choice in Rats

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Pain-related factors increase risk for opioid addiction, and pain may function as a negative reinforcer to increase opioid taking and seeking. However, experimental pain-related manipulations generally do not increase opioid self-administration in rodents. This discrepancy may reflect insufficient learning of pain-relief contingencies or confounding effects of pain-related behavioral impairments. The goal of this study was to determine if pairing noxious stimuli with opioid self-administration would promote pain-related reinstatement of opioid seeking or increase opioid choice over food.
Methods: In Experiment 1, male rats (n=11) self-administered fentanyl in the presence or absence of repeated intraplantar capsaicin injections in distinct contexts to model context-specific exposure to cutaneous nociception. After capsaicin-free extinction in both contexts, we tested if capsaicin would reinstate fentanyl seeking. In Experiment 2, male and female rats self-administered heroin after intraperitoneal (i.p.) lactic acid injections (n=13) to model acute visceral inflammatory pain or vehicle injections (n=7). After lactic acid-free extinction, we tested if lactic acid would reinstate heroin seeking. In Experiment 3, we tested if repeated i.p. lactic acid (n=8) or intraplantar Complete Freund's Adjuvant (CFA; to model sustained inflammatory pain; n=8) would increase fentanyl choice over food in male and female rats.
Results: In Experiments 1-2, neither capsaicin nor lactic acid reinstated opioid seeking after extinction, and lactic acid did not increase heroin-induced reinstatement. In Experiment 3, lactic acid and CFA decreased reinforcement rate without affecting fentanyl choice.
Conclusions: Results extend the range of conditions across which pain-related manipulations fail to increase opioid seeking in rats and suggest that enhanced opioid-addiction risk in humans with chronic pain involves factors other than enhanced opioid reinforcement and relapse.
Financial Support: This work was supported by NIDA/NIH.

M92. Long-Term Recovery From Opioid Use Disorder: Identification of Recovery Subgroups and Their Association With Opioid Use, Treatment, and Quality of Life

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research

Aim: Limited information exists regarding subgroups of individuals in recovery from opioid use disorder (OUD) following treatment, and how these subgroups may relate to key outcomes. We utilized a data driven approach to identify important dimensions of recovery, characterize recovery subgroups, and assess their association with opioid use, treatment utilization, and quality of life.
Methods: N=216 individuals enrolled in the Remission from Chronic Opioid Use-Studying Environmental and SocioEconomic Factors on Recovery - Long Term (RECOVER-LT) study (NCT04577144). RECOVER-LT is a single 4-year follow-up assessment of individuals with OUD who participated in a 2-year observational study (NCT03604861) following enrollment in a phase 3 clinical program. We used Principal Component Analysis on psychosocial and opioid dependence variables to identify dimensions of recovery in this sample. Next, we used k-means clustering to classify individuals into distinct recovery subgroups.
Results: Three dimensions of recovery were identified: Depression, Opioid withdrawal, and Pain. k-means clustering identified four recovery subgroups stratified by these dimensions: High-functioning (minimal depression, mild withdrawal, no/mild pain), Pain (minimal depression, mild withdrawal, moderate pain), Depression (moderate depression, mild withdrawal, mild/moderate pain) and Low-functioning (moderate depression, moderate/severe withdrawal, moderate/severe pain). Recovery subgroups were associated with important outcomes including DSM-5 criteria ($p<0.001$), remission status ($p<0.001$), recent opioid use ($p<0.001$), treatment utilization ($p<0.001$), and physical health, psychological, environment and social relationship quality of life domains ($ps<0.001$).
Conclusions: We identified three novel dimensions of recovery from OUD, synthesized these dimensions, and characterized four distinct recovery subgroups. These subgroups aligned with OUD diagnostic criteria and were associated with contemporaneous opioid use, treatment utilization, and quality of life outcomes. These results highlight the multidimensional, individualistic nature of OUD recovery and emphasize the need for personalized addiction medicine.
Financial Support: This work was supported by Indivior, Inc., North Chesterfield, VA, USA.

M93. Multidimensional Assessment of Access to Medications for Opioid Use Disorder Across Urban and Rural Communities: A Scoping Review

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Literature Review
Aim: According to the patient-centered access to healthcare framework, access to healthcare is a multidimensional phenomenon impacted by five healthcare system dimensions (approachability, acceptability, availability and accommodation, affordability, appropriateness), and five patient ability dimensions (ability to perceive, seek, reach, pay, engage). Interventions to improve local access to medications for opioid use disorder (MOUD) require an understanding of how these dimensions differ across urban and rural areas. Therefore, we systematically appraised the literature on access to MOUD across urban and rural communities (i.e., urbanicity) using this conceptual framework.
Methods (Optional): We performed a scoping review of 1) electronic databases, 2) grey literature, and 3) correspondence with content experts (March 2021). We included articles defining the study sample by urbanicity and examining at least one dimension of access to MOUD. We excluded studies outside the U.S. or not in English. Article screening and data extraction were completed by two authors and disagreements resolved by a third. The analysis and qualitative synthesis of study results examined study characteristics, key findings, and categorized articles by dimensions of access.
Results (Optional): The search produced 3283 unique articles, of which 124 met inclusion criteria. Two dimensions of access were most frequently assessed: availability and accommodation (57%) and acceptability (23%). Less than 20% examined any of the five dimensions of patient ability. Additionally, less than half of studies made comparisons by urbanicity (46%) and nearly half did not use a standard measure to define urbanicity (46%).
Conclusions: Only two healthcare system dimensions of MOUD access were frequently examined within the existing literature and few studies make comparisons by urbanicity or prioritize the patient's perspective,

limiting our understanding of how access differs by urbanicity. As the COVID-19 pandemic spurs expansion of telehealth and other changes in MOUD delivery, research into other dimensions of access is needed, particularly from the patient perspective.
Financial Support: Supported by NIDA 5K12DA033312-17

M94. Prevalence of Mental Disorders Among People With Opioid Use Disorder: A Systematic Review and Meta-Analysis

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of our systematic review and meta-analysis was to synthesise evidence on the prevalence of mental disorders among people with opioid use disorder (OUD). We estimated the prevalence of depression, anxiety, posttraumatic stress disorder (PTSD), bipolar disorder, personality disorders, attention-deficit disorder (ADD), and other pre-specified mental disorders among people with OUD.
Methods: We searched Embase, MEDLINE, and PsycInfo to identify studies of people with OUD with mental disorder data from January 1990 to July 2021. Observational studies that evaluated one or more mental disorder through clinical diagnosis or validated scales were included. We extracted the current and lifetime prevalence of each mental disorder, sample characteristics, and methodological factors from each publication. Random-effects meta-analyses were used to pool prevalence estimates for each disorder with 95% Confidence Intervals (95% CIs). Meta-regressions and stratified meta-analyses were used to assess variance in mental disorder prevalence estimates by sample and methodological characteristics.
Results: Of the 36,971 publications identified, we included data from 345 studies and 104,135 people with OUD in at least one pooled estimate. Among people with OUD, the prevalence of current depression was 36.1% (95% CI 32.4-39.7%), anxiety was 29.1% (95% CI 24.0-33.3%), ADD was 20.9% (95% CI 15.7–26.2%), PTSD was 18.1% (95% CI 15.4-20.9%), and bipolar disorder was 8.7% (95% CI 6.7-10.7%). Lifetime prevalence of anti-social personality disorder was 33.6% (95% CI 29.1-38.0%) and borderline personality disorder was 18.2% (95% CI 13.4-23.1%). Sample characteristics and methodological factors, such as participant sex and recruitment methods, were associated with significant differences in pooled estimates for specific disorders.
Conclusions: Mental disorders are far more common among people with OUD than the general population. Our findings may inform clinical guidelines, treatment services, and future studies that aim address the needs of people with OUD.
Financial Support: The National Drug and Alcohol Research Centre (NDARC; UNSW Sydney) is supported by funding from the Australian Government Department of Health under the Drug and Alcohol Program. TS is supported by higher degree research scholarship from the NDARC. LD and GC, are supported by Australian National Health and Medical Research Council (NHMRC) research fellowships (#1135991, #1119992). LD receives support from a US National Institute of Health (NIH) National Institute on Drug Abuse (NIDA) grant (R01DA1104470). LTT is also supported by this grant. NG is supported by a UNSW Scientia Fellowship. SC and JW acknowledge PhD scholarship funding from the National Health and Medical Research Council. SC acknowledges UNSW Scientia Scholarship funding schemes. The funders had no role in the design, data collection, analysis, interpretation of findings, or article submission.

M95. Project RIDE: Accessible and Acceptable Mobile Strategy for Community-Based Moud Engagement

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human

Abstract Category Original Research
Aim: RIDE evaluates the impact of a team (nurse practitioner, peer recovery specialist, case manager) that delivers a transitional buprenorphine/naloxone treatment from a mobile research facility as a method for linking individuals to community based MOUD treatment.
Methods: Descriptive analyses at baseline and 6-month follow-up of participants recruited at the mobile unit versus at the Crisis Response Center (CRC).
Results: The sample consisted of 104 participants, who met severe opioid use disorder (OUD) criteria and who sought treatment for OUD in the mobile unit (Intervention, n=55) or at the CRC (Control, n=49). Participants were mainly males (79.2%), 39.2 y.o., 68.3% White, 23.1% Black, 22.1% Latin(x), polydrug users, and in economic distress. There was no difference between the two groups. Prior to COVID-19 restrictions, most interventions and medication delivery occurred on the mobile unit parked in neighborhoods with high prevalence of opioid overdoses. Because of COVID-19 restrictions, remote services and medication delivery were used extensively. These remote services have been highly rated by the participants. These changes provided opportunities to participants who would not have been engaged in treatment otherwise (home arrest, injuries, lack of money to go to the mobile unit). At 6-month follow-up, among those able to be contacted, 62.5% of the participants of the Intervention group were engaged in MOUD in the community, versus 4.2% of the participants enrolled at the CRC. COVID-19 did not significantly impact the engagement in community treatment. Time to enter community-based treatment was not significantly impacted by COVID-19 (26 days pre-COVID, 31 days during COVID-19).
Conclusions: These findings suggest that a treatment delivery model that combines mobile and remote services to engage people living with OUD in community-based treatment is accessible and acceptable. The cost and sustainability of this strategy needs to be evaluated.
Financial Support: CDC R01CE003049

M96. Prospective Associations of Tobacco Use With Prescription Drug Misuse Among Young People

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The use of tobacco, especially cigarettes and e-cigarettes, remains a widespread problem among youth and young adults throughout the United States. Studies have showcased a link between tobacco use and prescription drug misuse. This study sought to provide further research on the prospective relationship between the use of cigarettes and/or e-cigarettes and prescription drug misuse among young people.
Methods: This investigation used restricted data from the Population Assessment of Tobacco and Health (PATH) study, a national longitudinal study examining tobacco use among adolescents and adults in the U.S. We utilized data from Waves 1-5 participants between the ages of 12 and 24 (n=60,658). Using Cox proportional hazards models, we examined prospective associations of time-varying tobacco use (e.g., cigarette, e-cigarette) with prescription drug misuse (i.e., painkillers, tranquilizers, and/or sedatives) on individuals who did not misuse prescription drugs at baseline.
Results: Young people who both smoked cigarettes and used e-cigarettes were 1.8 times more likely (95% CI:1.2, 2.5) to subsequently misuse prescription drugs, while those who only smoked cigarettes were 2.5 times more likely (95% CI: 2.0, 3.1) to misuse prescription drugs compared to those who did not use tobacco. For individuals who only used e-cigarettes, there was no association with subsequent prescription drug misuse (Hazard ratio=1.0; 95% CI: 0.7, 1.4).
Conclusions: This study suggests that tobacco use in young people, particularly smoking cigarettes or a combination of cigarette and e-cigarette use, may serve as an important indicator for future prescription drug misuse.
Financial Support: This work was supported by the National Institute on Drug Abuse and the US Food and Drug Administration (FDA) Center for Tobacco Products (R21DA051388) and Indiana University start-up funds (MAP).

M97. The Use of PICC Lines for Treatment of Serious Infections in People Who Inject Drugs: Review and Commentary

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Literature Review
Aim: Serious infections represent one of the most common reasons people who inject drugs (PWID) seek out healthcare. Standard of care for treatment of these infections includes protracted courses of intravenous (IV) antimicrobials - necessitating long-term IV access via peripherally inserted central catheter (PICC). Due to concerns for PICC misuse and potential complications including thrombosis, infection, overdose and death, professional society guidelines describe PWID as "poor candidates" for PICC lines, and providers describe being less likely to use PICC lines for treatment in PWID. To inform clinical practice and identify priorities for future research, this scoping review and commentary aims to characterize current literature regarding PICC line use among PWID, including rates of compliance and misuse, potential harms, and interventions to improve treatment outcomes.
Methods (Optional): MEDLINE and Embase databases were searched through December 22, 2021 using relevant MeSH terms or keywords, without date limitations. Inclusion criteria included citations 1) in English 2) describing PICC use for treatment of serious infections in PWID.
Results (Optional): We identified and reviewed the abstracts of 327 studies. Of these, 98 were selected for full text review, and 24 for data extraction, which is ongoing. Though several studies have examined compliance of PWID with treatment via PICC line, reported rates of PICC misuse in this population are often based on provider suspicion, with limited research characterizing patient experiences and practices. No studies to date have evaluated the potential effect of evidence-based treatments for substance use disorder (e.g., medication-assisted therapy) or harm reduction strategies on treatment outcomes.
Conclusions: Further research is needed to investigate potential effects of addiction treatment and harm reduction interventions on PICC line outcomes among PWID. More comprehensive understanding of patient experiences and practices may help to identify strategies to decrease perceived or real risks of PICC line use among this population.
Financial Support: NIDA grant R25-DA037756

SBIR POSTER SESSION (SMALL BUSINESS INNOVATION RESEARCH - SBIR)

Novel Digital and Behavioral Health Platform That Combines Opioid Compliance Protocols to Improve Prescriber Confidence, Reduce Liability, and Improve Patient Outcomes

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Drug Category Opiates/Opioids
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Inadequate training on how to properly initiate, monitor, continue and discontinue opioid therapy and fear of criminal, civil, and regulatory intervention has led many well-intentioned physicians to refuse to prescribe opioids altogether. As a result, clinics that do prescribe opioids have been inundated with patients almost out of medication or in withdrawal and many patients have turned to fentanyl and other synthetic opioids to relieve their pain. The objective of this research is to validate the protocols and delivery system of a novel digital Behavioral Health self-assessment platform by measuring patient outcomes, prescriber confidence, and completeness of documentation in the patient chart.
Methods (Optional): A total of 46 primary care and pain management clinics were randomized to one of two groups: a 1 hour continuing medical education (CME) course or a 1 hour CME course and the Care Continuity Program (CCP). The CCP is a software platform that informs opioid prescribers of patient therapy benefits and risks of misuse and creates standardized chart documentation. Patients complete the CCP self-assessment before every medical appointment. Results are instantly appended to the Electronic Medical Record (EHR) and providers review the information to inform their prescribing decisions. After 4

months, medical records from both groups are abstracted and patient outcome data (i.e., morphine milligram equivalents, physical functioning) and provider risk data (i.e., adherence to requirements for including certain data elements in medical record) are compared between groups. Provider confidence is also compared between groups in a pre and post intervention survey.
Conclusions: There is an urgent need for digital health technologies to identify patients at high risk for misuse of opioids, improve providers' confidence to manage chronic opioid therapy, and reduce providers' exposure to liability. The results of this project will determine whether the CCP software is beneficial in battling the opioid epidemic.
Financial Support: NIDA SBIR Grant Number 1R44DA051272-02

Development of a Digital Application for Patient Self-Management of Opioid Use Disorder: KIOS

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Drug Category Opiates/Opioids
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Original Research
Aim: Self-management of opioid use disorder (OUD) is an important object of substance use treatment. However, many patients receiving opioid agonist treatment have insufficient access to counseling support and social support between clinical visits. We developed a unique, patient-centered computational software system (KIOS) based on nonlinear methods to assist in managing OUD.
Methods: KIOS tracks interacting symptoms to determine the patient's individual trajectory then provides specific behavioral advice to help the person manage their unique levels of craving, depression, anxiety, and other self-reported symptoms. KIOS also provides analytics that can be used by clinicians and researchers to track outcomes. A total of 15 methadone-maintained OUD participants completed a 4-week acceptability and utility pilot study of KIOS.
Results: Participants completed 191 assessments averaging 13 assessments per user. The study population was diverse and comprised of 47% White (Non-Hispanic), 21% White (Hispanic), 10% more than one race, 10% American Indian/Alaska Native, 5% Black, and 5% Asian. Sixty-three percent of the participants were women, and the mean age of all participants was 34.4 years. At 4 weeks, use of KIOS was associated with significant reductions in opioid craving (-36%, $p<.05$), the KIOS Index score (-37%, $p<.05$), and other symptom categories associated with OUD treatment outcomes compared to baseline scores. Usability and generated advice received high assessment scores.
Conclusions: KIOS use was associated with a very positive user experience, reduction in opioid craving, and other symptom improvement. KIOS may be useful to augment in-person treatment of patients receiving opioid agonist treatment and help fill treatment gaps that currently exist in the continuum of care.
Financial Support: V. King, J. Potter, H. Priesmeyer, G. Siegel, L. Siegel are supported by NIDA grant 9 R42 DA054881-02 to develop KIOS for commercial use.

Development of CP-Analogs as Novel Treatments for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Molecular Pharmacology
Abstract Detail Animal Study
Abstract Category Program Descriptions
Aim: Sparian Biosciences is a development-stage CNS-focused biopharmaceutical company. Currently, we have 4 programs addressing various aspects of the opioid crisis.
Background: Opioid Use Disorder (OUD) is a chronic disorder characterized by the repeated and compulsive use of opioids. OUD is a global problem but is at crisis levels in the US, where it is estimated that 9.5M people misuse opioids, 2.7M have OUD, and >75K die annually from opioid-related overdoses. Mitragyna speciosa, a plant commonly known as Kratom, is widely used in the US as an herbal self-remedy to treat opioid withdrawal and OUD. We have identified and synthesized a distinct NCE based on the

structure of mitragynine, named 9-methoxy corynantheidine pseudoindoxyl (9CP). 9CP has a different receptor binding profile and pharmacology than mitragynine. 9CP is a partial MOR agonist and full DOR antagonist. In dosing studies 9CP attenuates precipitated withdrawal in morphine dependent mice, does not promote rewarding behavior or cause physical dependence, and demonstrates limited respiratory depression and tolerance.
Develop an oral, potent and selective 9CP analog for the treatment of OUD, devoid of unwanted side effects, and with a better pharmacotherapeutic profile than either buprenorphine or methadone. We will conduct lead optimization by synthesizing derivatives of 9CP and screening them via in vitro ADME, in vivo PK, and in vivo efficacy assessments. We will select our clinical lead, initiate CMC development, and perform initial exploratory tox studies to prepare for IND-enabling studies.
Conclusions: We plan to develop a novel 9CP analog for the treatment of OUD. Our 9CP analog aims to expand beyond the clinical benefit of Kratom in the form of an FDA-approved product and offer a treatment advance over buprenorphine and methadone.
Financial Support: Supported By: Fast-track SBIR grant from NIDA (1R44DA053846-01).

Rae (Realize, Analyze, Engage): A Digital Detection and Intervention for Individuals in Recovery from Substance Use Disorder

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Original Research
Aim: 1) Deploy and optimize an mHealth system in a population in treatment for substance use disorder (SUD); and
2) Evaluate the accuracy of craving and stress detection using a commercial grade wearable
Methods: The RAE system (wearable device and smartphone application) uses continuously measured physiologic data to detect stress and craving, identify him risk moments, and deliver real-time behavioral interventions. Craving and stress detection algorithms were developed on a research grade device (Empatica E4), but, for the purposes of this study, data were collected with an off-the-shelf wearable (Garmin Vivosmart 4). Adult subjects in outpatient treatment for SUD were asked to use the RAE system for 30 days and self-identify stress and craving episodes, while continuously collecting physiologic data (e.g. heart rate, and accelerometry). Descriptive statistics were calculated for app usage metrics. The previously derived bagged trees machine learning algorithm was applied to physiologic data, and test characteristics (accuracy and AUC for the ROC curve) were calculated.
Results: Fifty subjects were enrolled over 18 months, with an average age of 42. Thirty-eight percent were female, and 60% completed the 30-day protocol. A particularly high attrition rate was noted from subjects with lower socioeconomic status (SES). The mean number of days using RAE was 14, and the mean number of hours of day of RAE use was 9.9. The accuracy of detection from the commercial sensor data was similar to that previously derived from Empatica E4 (71.0 % (AUC= 0.74) vs 74.5 % (AUC=0.81) for stress and 71 % (AUC= 0.74) vs 75% for craving (AUC = 0.82)).
Conclusions: The RAE system was successfully deployed in adults in outpatient treatment for SUD, with higher compliance in higher SES subpopulations. Accuracy of stress and craving detection were similar using an off-the-shelf wearable sensor. Additional work to tailor the user experience of RAE is ongoing.
Financial Support: NIDA/NIH (R44DA046151)

Introduction to NIDA's Office of Translational Initiatives and Program Innovations (OTIPI)

Christopher Conrad*[1], Julia Berzhanskaya[1], Sara Lioi[1], Stacie Gutowski[1], Tamara Slipchenko[1], Tam Nguyen[1], Yordan Kostov[1], Victor Prikhodko[1], Leonardo Angelone[1], Elena Koustova[1]
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Drug Category Other, Small business
Topic SBIR/STTR

Abstract Detail Human
Abstract Category Program Descriptions
Aim: The NIH Small Business program includes the 24 NIH Institutes and Centers to fund scientists and entrepreneurs with a set aside $1.2 billion in non-dilutive funds every year -- specifically to support early-stage small business research and development. As part of the NIH, the Office of Translational Initiatives and Program Innovations (OTIPI), at the National Institute on Drug Abuse (NIDA), manages NIDA's small business program. Historically, due to stigma and competing market forces, there has been little investment from private industry into the developing startups within the SUD ecosystem as compared to other indications. Given this perpetual situation, academic SUD scientists need to play a more significant and extended role to champion their discoveries and ideas from the early stage to the market. NIDA's OTIPI strategic mission includes investing more effort and resources supporting small businesses/startups and entrepreneurially minded academic SUD scientists. OTIPI budget (>$40 million of NIDA's total budget), and Staff (e.g., Drug Development, FDA Device Development, Health IT) implement funding initiatives (e.g., Step Up for SUD: A Drug Target Initiative for Scientists Engaged in Fundamental Research), challenges (e.g., Start a SUD Start up), and the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs as a key part of NIDA's mission to foster "champions" to turn discovery into health. With NIDA OTIPI's financial and collaborative support, several exemplar companies have gone on to be financially self-sufficient in the multiple SUD areas including FDA regulated Devices, (e.g., Pair Therapeutics raised $396 million), pharmacotherapeutics (e.g., Blue Therapeutics raised $31 million), and Health IT (e.g., OpenBeds was recently acquired).
Conclusions: In conclusion, bringing SUD-related products to market is, for multiple historical reasons, the responsibility of NIDA scientist "champions". OTIPI is standing by, ready to help at every stage, from idea validation to FDA interactions and finally to reimbursement.

Mobile Brain Sensing Platform for Detection of Opioid Craving and Treatment Response

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Drug Category Opiates/Opioids
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Program Descriptions
Aim: A critical barrier for clinicians who treat OUD patients is a lack of FDA-cleared devices to identify valid disease biomarkers and educate patients on brain vulnerabilities for future craving and relapse. Neurofeedback enables patients to recognize OUD neurophysiology, and neurofeedback biomarker metrics may provide useful quantitative endpoints for tracking the effectiveness of OUD treatments. Neurotype Inc. is developing NeuromarkR, a neurofeedback device designed for OUD treatments that may motivate patient engagement by enabling identification of brain vulnerability biomarkers, and tracking progress with objective recovery benchmarks at the point of care.
Methods (Optional): In a recent SBIR Phase I project funded by the National Institute on Drug Abuse, we successfully demonstrated NeuromarkR's proof-of-concept in measuring neurophysiological biomarkers from more than 9 recently abstinent OUD inpatients (data collection ongoing) using portable wireless electroencephalogram (EEG) headsets in a hospital office. NeuromarkR's patent-pending system quantifies the extent to which Event-Related Potential (ERP) brain responses elicited by opioid cues (e.g., images containing a syringe, pill bottle, etc.) resembles brain responses elicited by naturally appetitive cues (e.g., erotica, palatable foods). This brain biomarker has been linked to deleterious treatment outcomes like relapse and treatment dropout in 20+ years of NIH-funded addiction neuroscience.
Results (Optional): The NeuromarkR system, anonymized patient reports, and other results from the SBIR Phase I project conducted with OUD clinicians and patients will be presented.
Conclusions: During the 2021 NIH Innovation Corps program, we showed NeuromarkR patient reports to clinicians and learned that NeuromarkR may satisfy outpatient OUD treatment providers' needs to aid establishing therapeutic alliance with new patients and sustain engagement with existing patients who are considering terminating treatment. A roadmap for further R and D guided by a 2021 FDA pre-submission meeting will be presented with regards to a planned De Novo marketing application for the NeuromarkR system and method.
Financial Support: R43DA053072

Integrating Augmented Reality (AR) and Immersive Learning Simulation (ILS) for Healthcare Training: Towards a Transmedia Solution to Address the Opioid Crisis

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Drug Category Opiates/Opioids
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Augmented Reality (AR) and Immersive Learning Simulation (ILS) technologies hold tremendous potential for transforming training and education for healthcare professionals and patients. While both AR and ILS have demonstrated an unprecedented level of success in a variety of healthcare training and education applications, particularly in the last few years, combining the two approaches remains a relatively uncharted territory. This is largely due to the relative lack of evidence-based methods, strategies, and practical guidance for the design and implementation of mixed reality and transmedia learning environments.
This presentation will discuss new integration strategies for bringing together AR and ILS technologies to provide a mixed transmedia learning experience for opioid overdose education, where the virtual and physical components seamlessly co-exist to create a new level of sophistication for education and training. The AR/ILS integration strategies will be presented within the context of an ongoing federally-sponsored research effort that aims to design, develop, and evaluate an innovative learning solution to help address the national opioid crisis with an ultimate goal of improving outcomes for people at risk for opioid misuse and overdose. Focusing on the training needs of healthcare professionals, first responders, and ordinary people (family members, caregivers, etc.) who are on the frontlines of the ongoing opioid crisis, the presented integrated AR/ILS solution illustrates how this transmedia approach can be used for training diverse learner audiences.
Conclusions: Based on this research effort, the presenters will share practical insights, lessons learned, and best practices for the design of comprehensive integrated AR/ILS-based solutions that can be easily applied to create effective and engaging learning experiences for a broad spectrum of training and education. The presenters will also elicit feedback from conference attendees on content and other application areas of interest to guide future research and implementation.
Financial Support: NIH/NIDA SBIR Award Number 2R44DA050371-02

Risk and Protective Factors for Initial Training Completion Among Substance Use Disorder Peer Worker Trainees

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: This study identifies potential risk and protective factors for completing classroom training among prospective peer worker trainees in Texas, building upon a preliminary evaluation of trainees in 2020.
Methods: Prospective trainees applied for a training scholarship (n=537) between January 14, 2020 and November 1, 2021, including both sexes. Eligible prospective trainees (n=425) provided demographic, life history, and recovery history information as part of the application (baseline), and a subset (n=241) completed an optional psychosocial survey at baseline measuring recovery capital, quality of life, self-stigma, and anxiety and depression. Three logistic regression models were used to identify potential risk and protective factors: a model assessing demographic, life history and recovery history variables' impacts on classroom training completion likelihood; a model assessing psychosocial impacts on completion likelihood; and a full model combining the two models.
Results: Previous use of a recovery community center (RCC) was associated with 2.6 times greater likelihood of completing classroom training (OR = 2.64, 95% CI [1.21,5.74]) in the first model more than

four times greater likelihood in the full model (OR = 4.14, 95% CI [1.22,14.07]). Identifying as Native American was associated with lower odds of completion (OR = 0.03, 95% CI [0.00,0.46]) in the first model. No psychosocial factors were associated with completion likelihood across models 2 (psychosocial factors only) or 3 (full model). A history of institutionalization was associated with lower odds of completion (OR = 0.36, 95% CI [0.13, 0.97]) in the full model.
Conclusions: Having a history of institutionalization emerged as a potential protective factor in a previous, preliminary analysis of trainees in 2020, but in this study emerged as a potential risk factor for attrition, highlighting the importance of continued research in this area. Previous use of RCCs emerged as a potentially strong protective factor in this study, reinforcing previous results.
Financial Support: This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $900,000 with 0 percentage financed with non-governmental sources (grant number T97HP33398). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS or the U.S. Government.

Identification of Epigenetic Biomarkers Associated With Prenatal Exposure to Substances of Abuse

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Original Research
Aim: The purpose of this project is to establish the feasibility of using epigenetic profiles to differentiate newborns with in utero illicit drug exposure and non-exposed newborns using neonatal blood spots. These perturbations to the epigenome could be used to identify which newborns are most at risk for developmental, neurodevelopmental, behavioral, and disease susceptibility later in life.
Methods: Our laboratory will identify a panel of the most differentially methylated regions (>5% DM) that are significantly associated with in utero exposure to a number of illicit drugs, based on whole-genome methylation analysis of DNA from infants known to have been exposed in utero and non-exposed controls. This panel will then be used to screen a sample (n= 150) of positive drug exposed and non-exposed neonatal blood spots to identify the epigenetic modifications that most significantly correlate with exposure to each drug and/or polydrug exposure. This analysis will include both sexes. We will establish the sensitivity and specificity of each methylation site and the predictive power of each single CpG site as well as possibly combinations of multiple CpG sites used together.
Results: This project is ongoing and the most recent results will be presented at this session.
Conclusions: Upon completion of this Phase I project we will have demonstrated the feasibility of using epigenetic modifications, in the form of DNA methylation patterns, to identify newborns at risk of fetal damage due to in utero exposure to a number of illicit drugs from neonatal blood spots. The goals of a Phase II study would be the development and implementation of a quantitative DNA methylation screening assay, the analysis of sites of differential methylation identified in this Phase I study, and to examine the correlation with both NAS severity and developmental outcomes in children enrolled in this study as they mature.
Financial Support: NATIONAL INSTITUTE ON DRUG ABUSE R43DA054030

Innovative Animal Experiment Design Tool

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Drug Category Other, preclinical testing of all drug types
Topic SBIR/STTR
Abstract Detail Animal Study
Abstract Category Original Research
Aim: We present a web application that guides researchers through the statistical experiment design process, recommending appropriate statistical analysis methods and sample sizes for animal experiments.

Methods: The application mysamplesize.com is built using Python and R programming languages. The application elicits basic information about treatments and other factors. The application uses well-established statistical computations to deliver power and sample size results for a variety of experiment scenarios, including repeated measures and post-hoc analyses. The application can also simulate experiments based on researcher inputs, so that researchers can explore the potential implications of their designs.
Results: The mysamplesize.com web application has been tested by a variety of biomedical researchers, who have found it easy to use and very helpful in preparing NIH applications. From simple two-group comparisons to repeated measures with multiple factors, mysamplesize.com can aid researchers in planning experiments.
Conclusions: With NIH asking for increased evidence of rigor in experimental design, the mysamplesize.com web application can help researchers with well-grounded statistical methods and sample sizes.
Financial Support: This research was supported by NIDA SBIR grant 5 R44 DA041760-03.

Multivalent Vaccine Strategies Against Polydrug Use in Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The number of annual fatal drug overdoses reached more than 100,000 between April 2020 to 2021, of which the majority involved individual opioids or polydrug mixtures containing opioids. A series of conjugate vaccines targeting fentanyl, carfentanil, oxycodone, heroin, and their analogs or metabolites have shown preclinical proof of efficacy, selectivity, and safety. Against polydrug use, the preclinical efficacy of multivalent vaccines was tested in mice.
Methods: Individual vaccines consist of haptens, small molecules that mimic the structure of the targeted drug, conjugated to carrier proteins, such as detoxified diphtheria toxin (CRM) or keyhole limpet hemocyanin (KLH). These studies identified lead haptens based on fentanyl (Fen), carfentanil (Carf), oxycodone (Oxy), and heroin (Her). In the current study, the male and female balb/c mice (n = 6) were vaccinated with a combination of Fen-CRM, Carf-CRM, Oxy-KLH, and Her-KLH as a quadrivalent vaccine. After the immunization, hapten-specific antibody IgG titers were tested using ELISA. The immunized mice were then challenged by the combinations of opioids. During the drug challenge, the efficacy of the vaccines was determined using oximetry to check heart rate and oxygen saturation, and hot plate assay to measure the latency of response as an indication of opioid-induced antinociception. To study the drug distribution, blood and brains were collected to measure the drug concentration using LC-MS/MS.
Results: ELISA showed that quadrivalent vaccine increased fentanyl-, carfentanil-, oxycodone-, and heroin-specific IgG titers in the immunized mice. Correspondingly, this simultaneous immunization prevented the distributions of fentanyl, carfentanil, oxycodone, and heroin to the brain when the mice were challenged by the mixture of these drugs.
Conclusions: These data demonstrate that individual efficacy of monovalent vaccine was preserved in a multivalent formulation without interference. Amid opioid epidemics, multivalent vaccine strategies will provide a broad spectrum of protection against multiple opioids with a single vaccination.
Financial Support: NIDA DA048386 (PI: Marco Pravetoni)

Overdose Deaths Involving Non-Bzd Hypnotic/Sedatives in the USA: Trends Analyses

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human

Abstract Category Original Research
Aim: There is sparse knowledge on overdose deaths resulting from nonbenzodiazepines and gabapentinoids usage. We examined overdose death rate across demographics categories and the overdose death trends over time.
Methods: Using data from the National Center for Health Statistics, we identified 21,167 persons that died with an overdose ICD code as the underlying cause of death and had a T42.6/T42.7 ICD code, which include gabapentinoids and z-drugs, among their multiple causes of death. The overdose death rate was calculated per 100,000 persons for every year between 2000 and 2018. We used joinpoint regression analyses to assess trends over time.
Results: We identified a rise in the proportion of deaths with a T42.6/T42.7 ICD code between 2000-2006 (yearly change: +0.06, $p<0.05$) and between 2006-2015 (yearly change: +0.32, $p<0.05$). From 2000 to 2008, the proportion of deaths with any other T code rose significantly (yearly change: +3.56, $p<0.05$). Between 2008 and 2018, there was also a significant rise (yearly change: +1.31, $p<0.05$). From 2000 to 2015, the proportion of deaths with a T42.6/T42.7 ICD code with any other T code rose (yearly change: +2.58, $p<0.05$). From 2000 to 2015, the proportion of deaths with a T42.6/T42.7 ICD code with a concurrent benzodiazepine T code rose (yearly change: +1.98, $p<0.05$). From 2000 to 2005, the proportion of alcohol T codes rose non-significantly (yearly change: +0.35). Finally, the proportion of alcohol T codes fell significantly between 2008 and 2018 (yearly change: - 0.74, $p<0.05$).
Conclusions: Deaths due to non-benzodiazepine hypnotics and gabapentinoids increased significantly over the last two decades. Clinicians should not assume that replacing benzodiazepines and opioids with these medications necessarily lowers risk to the patient.
Financial Support: Columbia University President's Global Innovation Fund (PI: Martins)

Technology Assisted Motivational Interviewing: Developing a Scalable Framework for Promoting Engagement With Tobacco Cessation

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Drug Category Nicotine/Tobacco
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Technology-assisted motivational interviewing (MI), driven by machine learning, may provide an efficient way to facilitate behavior change and support an innovative program of SUD research. This study developed the Technology Assisted Motivational Interviewing (TAMI) Coach, a digital conversational agent that incorporates machine learning models to deliver MI for tobacco cessation and provide tailored referrals to treatment.
Methods (Optional): Transcribed MI sessions were obtained from collaborators and coded for change talk (CT) and sustain talk (ST). 20,890 coded utterances were then broken down into words and subwords for machine learning model training. In order for TAMI to respond to a variety of smoking-related conversational topics, 14,106 unique utterances were also extracted from 81 subreddits to create a topic classification model with 81 topics. Once ensemble methods considering large scale pre-trained language models, such as BERT, RoBERTA, and XLNet, were fine-tuned, a logical framework was built to guide the MI session through a series of rules, while adapting to the user's stage of change and topic of interest. A tailored referral system was also created that allows the prepared user to select quit tools (e.g. NRT, behavioral counseling) and develop a fully tailored, actionable quit plan.
Conclusions: Both the machine learning classifiers (CT, ST, and topic) and the tailored referral architecture have demonstrated strong performance during initial testing and are being further evaluated in a feasibility and acceptability pilot RCT. TAMI explores motivation and ambivalence associated with tobacco use, employs interventions to elicit CT, evaluates readiness for tobacco cessation, and facilitates detailed quit plans and referrals to treatment when appropriate. TAMI's architectural framework and "training" methods are readily adaptable to other substance use behaviors and may support a rich area of digital health research in SUD.
Financial Support: This project was supported by the California Tobacco-Related Disease Research Program.

Small Business Program: Patient Uptake and Use of a Technological Solution to Support Treatment for Opioid Use Disorder in the Primary Care Setting

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Drug Category Opiates/Opioids
Topic SBIR/STTR
Abstract Detail Human
Abstract Category Original Research
Aim: Patients receiving medication for opioid use disorder (MOUD) often face challenges in adhering to their treatment regimens. Technological solutions offer the potential to improve patient access to their providers; however, patterns relating to patient uptake and use of such solutions over the course of their treatment has been under explored. The Opioid Addiction Recovery Support (OARS) software enables patient connection to their healthcare provider through a patient mobile application and provider portal. We sought to describe uptake and patterns of OARS use among patients at a large suburban primary care provider in Northeast Pennsylvania.
Methods: The OARS platform was deployed for widespread use for all patients receiving MOUD from May to November of 2021. After patients downloaded the mobile app and signed up for an account data were uploaded from the electronic health record to the OARS platform on a weekly basis.
Results: Through the first three months of OARS deployment, only 20% of patients downloaded the app and created an account; however, case manager consultation increased OARS uptake to 45% after six months. Among 172 patients who signed up for OARS, 80% used the patient app. No age, sex, or race/ethnicity differences were observed between users and non-users. Most app users were 30-49 years old (69%), 56% were male, and 86% were white. The OARS system recorded 1592 interactions where viewing urine toxicology test results was the most popular feature (25% of all interactions) followed by progress views (10%) and sending messages to providers (8%).
Conclusions: While uptake of the OARS technology was at first limited, patients were more inclined to download OARS after consulting case managers. Use of OARS varied widely by patients over the course of their treatment. More exploration is needed to determine factors associated with uptake and use of technological solutions to support MOUD.
Financial Support: Supported by NIH Grant # 1R42DA05039898-01

Virtual Opioid User: Reproducing Opioid Use Phenomena With a Control Theory Model

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Drug Category Opiates/Opioids
Topic Tolerance/Dependence
Abstract Detail Human
Abstract Category Original Research
Aim: To develop a control theory model capable of reproducing pathways to opioid use disorder under different dosing conditions and individual characteristics, as well as a web application allowing users to interact with the model.
Methods: We developed a model to simulate an individual's opioid use over 15-minute time steps for several years. We followed the principles of control theory and opponent-process theory, formalizing representations of several processes. Opioid concentration was modeled with a pharmacokinetic decay equation calibrated to morphine plasma half life. Several other processes were modeled as a series of weighted integrals:
- Habit, representing the individual's adjustment to past use,
- Effect, representing how the individual perceives opioid use, and
- Craving, motivating the individual to use.
Parameters affecting the individual's opioid use trajectory include starting dose, opioid availability, dose variability (including the adulteration of illicit opioids), and individual and social risk propensity to opioid use. These processes govern when the individual takes opioids, increases their preferred dose, and

overdoses. We developed an open-source web application allowing users to explore how dose variability and other model parameters affect the individual's opioid use over time.
Results: Our model reproduced four target phenomena:
- Maintenance of low dose without craving or dose increase,
- Gradual increase of dose at medium doses,
- Rapid increase of dose and craving at high doses, and
- Increased craving during subsequent periods of abstinence.
Conclusions: Our computational model creates the basis for a natural history of opioid use, which is critically needed to understand policy implications at the individual level. Our web application could be used by clinicians to explore how internal and external factors can affect the dynamics of opioid use. We have demonstrated that a relatively simple control theory approach can reproduce many of the key characteristics of real-world opioid use.
Financial Support: Funded by NIDA grant 5R01DA047994-02

TUESDAY, JUNE 14, 2022

POSTER SESSION 3

T1. Arkansas Treatment Admission Trends From 2000 to 2020 for Dual Opioid-Methamphetamine or Opioid-Cocaine Use Problems

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Drug overdose deaths continue to be a major public health problem and appear to be driven not only by opioid, but also, more recently, illegal stimulant use. This study examined longitudinal changes in treatment admissions for opioids (OP) as the primary drug problem and methamphetamine (MA) or cocaine/crack (COC) as the secondary or tertiary drug problem and vice versa in the state of Arkansas from 2000-2020.
Methods: Data for substance use treatment admissions from all programs receiving federal funds from 2000 to 2020 were extracted from the Arkansas (AR) Alcohol Drug Management Information System (ADMIS). Cochran-Armitage test for trends was used to determine any longitudinal changes in percentage of admissions per year for: OP as primary, MA as secondary/tertiary drug problem (OP/MA); OP as primary, COC as secondary/tertiary drug problem (OP/COC); MA as primary, OP as secondary/tertiary drug problem (MA/OP); and COC as primary, OP as secondary/tertiary drug problem (COC/OP).
Results: The percentage of OP/MA admissions increased from 6.1% in 2000 to 28.6% in 2020 ($z= -29.03$, $p<0.0001$). OP/COC admissions decreased from 8.0% in 2000 to 1.1% in 2020 ($z= -28.92$, $p<0.0001$). MA/OP admissions increased from 1.4% in 2000 to 15% in 2012 followed by a levelling off/slight decrease to 10.8% in 2020 ($z=19.53$, $p<0.0001$). COC/OP admissions increased from 0.9% in 2000 to 7% in 2008, followed by a levelling off/decrease to 0.3% in 2020 ($z=-9.34$, $p<0.0001$).
Conclusions: The patient base involving OP use has shifted, with a significant increase and decrease over time in treatment admissions for OP/MA and OP/COC, respectively. Changes in the percentage of admissions for MA/OP and COC/OP over time have been more complex, with initial increases, followed by leveling off or decreases in admissions. These findings suggest that effective treatment strategies addressing dual OP and MA use are particularly needed.
Financial Support: Supported by SAMHSA grants H79TI083287 and 6H79SP080990 to Arkansas Department of Human Services/Division of Aging, Adult, and Behavioral Health Services

T2. Childhood Neglect Predicts Perceived Quality of Care in Patients With Co-Occurring Substance Use and Mental Disorders

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Childhood trauma is associated with increased risks for long-term mental health problems, including greater drug use and poorer psychosocial functioning. Despite the high prevalence rate of childhood trauma among patients with mental health and substance use disorders (SUD), few studies have examined challenges in treatment associated with past childhood maltreatment. This study investigates the relationship between childhood trauma and perceived quality of care in patients undergoing drug use and mental health treatment.
Methods: 259 inpatients with co-occurring mental health and SUDs (36.3 ±11.1 years old; 86F) were recruited after ≥1 months of admissions. Participants completed a single session comprising self-report questionnaires, including the Childhood Trauma Questionnaire-Short Form (CTQ-SF) and the Inpatient Consumer Survey (ICS). Six ICS subscales (Outcome Care, Dignity, Rights, Empowerment, Environment, Engagement) were individually regressed on 6 CTQ subscales (Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, Physical Neglect, Minimization/Denial). Diagnoses and drug use were retrieved via patient chart review.
Results: All patients presented with SUD, 55% from multiple SUDs. Prevalence of psychiatric diagnoses were 51% psychotic, 27% mood and 34% neurodevelopmental disorders. Emotional Neglect and Minimization/Denial independently predicted poorer ratings across all ICS subscales (ps<.05). Physical Neglect independently predicted poorer ratings across all ICS subscales (ps<.05), except Rights and Environment. There were no other relationships between childhood trauma and inpatient consumer responses. Significant CTQ predictors were not correlated with psychiatric diagnoses or SUDs.
Conclusions: Childhood neglect but not childhood abuse was associated with an increased likelihood of negative experiences with treatment care. This is the first data to suggest history of childhood neglect is a potentially important contributor to treatment challenges in patients with severe concurrent disorder. Further investigation is needed to assess past childhood neglect and quality of care and their relationship with treatment outcomes.
Financial Support: Funding support for this project was provided by the Canadian Centre for Substance Use and Addiction. The authors have no conflicts of interest to disclose.

T3. Craving-Manager App Designed to Manage Craving and Individual Predictors of Substance Use / Addictive Behavior in Addiction: A Randomized Controlled Trial Study Protocol

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Program Descriptions
Aim: The proportion of individuals with addiction who are currently treated is low (<10%). Barriers such as stigma, desire to cope alone, difficulty to access treatment could be overcome by mobile technologies. EMI (Ecological Momentary Intervention) is a treatment procedure characterized by the delivery of interventions (messages on smartphones) to people in their daily lives, when it is most needed.
Craving is a strong predictor of relapse and a key target for addiction treatments. Previous EMA studies have revealed that, in daily life, person-specific cues could precipitate craving, that in turn, is associated with a higher probability to report substance use in the following hours. Thus, assessment and management of these specific situations in daily life could help to decrease use and avoid relapse.
Craving-Manager app was designed for all addictions (substances/addictive behaviors) to assess and manage craving and person-specific cues, and to deliver specific and individualized interventions (counseling messages), based on validated cognitive-behavioral psychotherapies for addiction.
The objective of this study is to evaluate the efficacy of using Craving-Manager app in decreasing use over 4 weeks, among individuals requesting, and waiting for initiation of outpatient addiction treatment.

Methods (Optional): 274 participants will be recruited in 6 outpatient addiction treatment centers in France, at their treatment request, and at least one month before the start of treatment.
This Randomized Controlled Trial will compare two parallel groups: experimental group (full interventional version of the application, 4 weeks, EMA + EMI), versus control group (restricted version of the application, 4 weeks, only EMA).
Conclusions: This new therapeutic tool will offer the possibility of an easy to-use and personalized intervention accessible to the greatest number of subjects.
Financial Support: PHRC-N 2018-0528 (M. Auriacombe, Charles Perrens Hospital)

T4. Development of the Stop Covid Today Intervention to Increase SARS-CoV-2 Vaccination Among People Who Inject Drugs

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: People who inject drugs (PWID) not only face dramatically greater risk of SARS-CoV-2 infection, they also face significantly increased danger of hospitalization and death from COVID-19. Unfortunately, due to stigma, the effects of systemic racism, and a lack of access to healthcare, PWID are less likely to be offered COVID vaccinations directly, many decline, and some remain strongly opposed to vaccination. The current proposal describes the collaborative development of a technology-based intervention designed to increase uptake of SARS-CoV-2 vaccination among PWID in East Harlem and the South Bronx, New York.
Methods: Researchers at NYU partnered with community-based organization New York Harm Reduction Educators to conduct two rounds of qualitative interviews with unvaccinated injectors (N=33) examining why PWID decline vaccinations when offered, and how digital media can potentially address barriers to vaccination. Monthly community advisory board (CAB) meetings were also convened to discuss vaccine hesitancy among PWID and strategies for intervention development. Iteratively drafted intervention components were then developed and evaluated by an additional sample of unvaccinated PWID (n=15) and via an ongoing clinical trial (N=500). Males and females were included in all phases of research.
Results: Our team created intervention components guided by Social Cognitive Theory and the Information, Motivation, Behavioral Skills Model. These include a brief 4K ultra high definition intervention video and follow-up SMS reminder messages specifically addressing barriers identified in qualitative interviews (e.g. fear of side effects, online misinformation, mistrust of government, etc.). Messages about protecting older relatives, children, and other community members facilitated vaccination.
Conclusions: The collaboration between researchers, CAB members, and PWID community members proved essential to our work, and provides a methodological example for additional projects targeting underserved populations and marginalized individuals. Interview data show PWID found pro-vaccination messages more credible when delivered by community members describing their own experience.
Financial Support: R01DA054990; P30 DA029926; P30 DA011041

T5. Difficulty in Emotional Regulation is Associated With HIV Risk Related to Drug Use

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Both difficulty in emotional regulation and adverse neighborhood environments have, separately, been associated with several types of risky behaviors. We examined both together in a cross-sectional sample of city dwellers.

Methods: 300 adults (61% male; 85% HIV-positive) from Baltimore, MD, completed the Difficulties in Emotion Regulation Scale (DERS), which produces six subscale scores (Non-acceptance, Goals, Impulse, Awareness, Strategies, and Clarity); the HIV Risk-Taking Behaviour Scale (HRTBS), which produces two subscale scores (past-month drug risks and sexual risks); and the Perceived Stress Scale. Participants' home neighborhood psychosocial hazards (social disorganization, public safety, physical disorder, economic deprivation) were scored using Baltimore Neighborhood Indicators Alliance data. Differences in HRTBS subscores were analyzed by linear regression.
Results: In bivariate analyses, there were positive associations between drug risk and several DERS subscales: Strategies, Goals, Awareness, and Clarity (.13 [.01–.25, 95% CI] < reffect < .18 [.06–.30]). The associations between drug risk and the other DERS subscales and between sexual risk and all DERS subscales were not significant (.00 [-.11–.11] < reffect < .08 [-.04–.20]). There were no significant effects of neighborhood hazard (all main effects and hazard X DERS interactions not significant). In multiple regressions controlling for age, gender, race, HIV status, and self-reported stress, only the association between drug risk and DERS Awareness was significant (reffect = .13 [.01–.25]).
Conclusions: People with greater difficulty with emotional regulation reported more HIV-risk behavior related to drug use but not sexual behavior, and this relationship was not impacted by their home neighborhood environment. Additional work is needed to determine why we did not find relationships with sexual behaviors, whereas previous literature found differences in both drug risk and sexual risk behaviors by emotional regulation. It may also be worth considering environmental contexts outside of the home neighborhood (e.g., activity spaces).
Financial Support: Supported by NIDA IRP

T6. Efficacy of Screening and Referral to Targeted Prevention That is Founded on the Liability-Threshold Model

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: Response to the opioid epidemic, other recent substance use (SU) endemics, and related drug overdoses have largely involved treatment and overdose prevention, with less development of primary prevention targeting high-risk youths. We hypothesized that SU among high-risk youths would be reduced by a well-child check-up screening and prevention (SAP) program for youths with high liability to early adolescent SU.
Methods: Founded on the liability-threshold model, screening indexed a range of risk factors (rather than querying SU per se) to detect (1) risk prior to SU initiation, (2) the full range of liability, and (3) liability to commonly co-occurring externalizing behaviors. Parents of at-risk youths were offered the Family Check-Up (FCU), a family-based intervention incorporating motivational interviewing and family management skills to address youth and family risk factors linked to early-onset SU and other problem behaviors. Screening occurred at ages 10-13 in boys and girls from low-resource communities of the Pittsburgh region. Of 361 screened and randomized families, 123 received the FCU and 238 were controls. About 80% of at-risk youths were African American, had a mean age of 11.93 (SD=1.17), and 32.4% had initiated SU. 12-month outcomes were available for 83.4% of families; missing data were multiply imputed. Efficacy was tested using PROC GLM and linear, Poisson, or negative binomial regression based on the outcome distribution, controlling for baseline differences between FCU and control families and baseline level of the outcome.
Results: Youths with greater baseline SU benefitted more from FCU in terms of fewer new substances initiated and less frequent SU. Additional FCU efficacy included reduced tolerance of deviance and anxiety but not for conduct disorder symptoms.
Conclusions: SAP with FCU reduces early adolescent SU and certain known risk factors for SU-related problems. Intervention impact for high-risk youths may be strengthened by specifically targeting conduct problems.
Financial Support: Supported by funding from NIDA (R01 DA036628).

T7. Gender Differences in Prescription Medication Misuse in Primary Care

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: The primary aim of the study was to analyze factors associated with prescription drug misuse (PDM) stratified by gender in a large, diverse sample of primary care patients.
Methods: Participants were N = 4,458 individuals recruited from urban primary care and gynecologic clinics for an anonymous health survey. Participants completed the survey on a tablet, guided by a 3-D avatar. The primary outcome was prescription medication misuse in the past month. Respondents were provided with a definition of misuse and examples. Self-identified gender was assessed with the options of "male" or "female." Correlates were selected based on literature review and availability of data, and included demographic variables, presence of chronic diseases, use of substances including alcohol, tobacco, and illicit drugs, family history of substance use problems, and mental health variables. Analyses were stratified by gender and associations between the outcome and correlates were tested via t-tests and Chi-square tests of independence. Gender-stratified, stepwise multivariate logistic regression (MLR) models were estimated with significant variables to find the most parsimonious PDM prediction models.
Results: The MLR models were significant overall for both men ($p<.001$) and women ($p<.001$). Among men, odds of past month PDM were higher with chronic pain (OR = 1.73), hepatitis (OR=1.78), positive alcohol screen (OR=1.58), mood disturbance (OR=1.04), and depression diagnosis (OR=1.77). Among women, odds of PDM were higher with recent illicit drug use (OR=2.22), positive alcohol screen (OR=2.66), family history of drug problems (OR=1.41), mood disturbance (OR=1.04), and heart disease (OR=0.48).
Conclusions: This study provides insight into the differential presentation of PDM between men and women. Not only did prevalence of PDM differ by gender, factors associated with misuse also varied. These findings help elucidate the context in which PDM occurs for men and women to better understand the clinical features of PDM and develop gender-informed prevention and treatment strategies.

T8. HIV Education, Awareness, and Referral and Treatment for Substance Use Disorders (HEARTS): A New Generation of Substance Use Treatment

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Program Descriptions
Aim: UT-HEARTS is a SAMHSA funded service project designed to address treatment for substance use disorders and provides education and testing for HIV and hepatitis C (HCV). UT-HEARTS strives to reduce disparities in not only addictions treatment but disparities in the number of racial/ethnic, sexual and gender minorities unaware of their HIV status. This program was developed to overcome these disparities by providing integrated treatment for substance use disorders that includes HIV and HCV testing, and linkage to care, as well as hepatitis A/B vaccinations, medication assisted treatment for opioid use disorders, and case management services. UT-HEARTS strives to increase awareness and access to addictions treatment for minority populations using a multidisciplinary approach that addresses prevention, assessment, diagnosis, and treatment. These professionals coordinate risk reduction and clinical services to help participants reach goals and overcome challenges that may interfere with treatment. Clinical services addressing addiction and co-occurring psychological disorders include assessment, diagnosis, and evidence-based individual counseling.
Results (Optional): The multidisciplinary treatment approach increases the likelihood that participants will achieve favorable outcomes and improve. As of 2021, UT-HEARTS has received more than 500 referrals

(n=505), and has provided services to 46% (n=235) of those referred. Provided services include individual counseling (n=150, 63.85%, HIV testing (n=82, 34.89%), and HCV testing (n=44, 18.72%). Despite a poor 6-month follow-up rate (n=59; 25.1%), favorable program outcomes were identified. A higher percentage reported abstinence (33.9%), and fewer reported past 30-day cocaine (18.6%), marijuana use (30.5%), condomless sex (40.7%), and injection drug use (3.4%).
Conclusions: A critical lesson learned in the early stages of the program was the importance of educating counselors about risks of HIV and hepatitis C associated with substance use. This helped counselors support at-risk clients who benefit from harm reduction services. Challenges include getting participants to complete three rounds of Hep A/B vaccinations, retention in treatment for opioid use disorder, and collecting six-month follow-up data.
Financial Support: Substance Abuse and Mental Health Services Administration (SAMHSA)

T9. Health Service Utilization Among Hospitalized Patients Experiencing Homelessness in a Randomized Clinical Trial of Patient Navigation Services

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: To examine rates of health service utilization among hospitalized patients experiencing homeless through 12-months of follow-up.
Methods: Participants (N=400) were hospitalized medical or surgical patients with a current diagnosis of opioid, cocaine, or alcohol use disorder enrolled in the Navigation Services to Avoid Rehospitalization (NavSTAR) study. Participants were randomized to either treatment-as-usual (TAU) or a patient navigation intervention. Health service utilization (inpatient admissions and emergency department [ED] visits) data were abstracted from the regionwide health information exchange through 12-months follow-up. We examined the association between health service utilization and baseline sociodemographic (including current housing status), substance use characteristics (opioid, cocaine, and/or alcohol use disorder), and study condition using multivariable negative binomial regression.
Results: At baseline, 43% of participants (n=172) reported experiencing homelessness (including unsheltered living and doubling up). In multivariable negative binomial regression, homelessness (Incidence Rate Ratio [IRR]=2.23 [1.63, 3.03] $p<0.001$) and alcohol use disorder (IRR=1.75 [1.19, 2.56] $p=0.004$) were associated greater incidence of ED visits through 12-months follow-up, whereas incidence of ED visits was lower among female participants (IRR =0.61 [0.46, 0.82] $p=0.001$). For inpatient admissions, patient navigation (IRR=0.74 [0.57, 0.95] $p=0.02$) was associated with decreased incidence of admission through 12-months follow-up. There was no significant association between homelessness and the incidence of inpatient admissions.
Conclusions: Hospitalized patients with comorbid substance use disorder and experiences of homelessness had higher rates of ED visits compared to those who were stably housed through 12-months of follow-up. Research on targeted interventions for hospitalized individuals experiencing homelessness are needed to improve their housing stability and engagement with non-emergency, community-based health services.
Financial Support: NIDA R01DA037942, NIDA T32DA007292

T10. Illegal Drug Use in Adolescents: A Missed Opportunity for Intervention in Taiwan

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research

Aim: In the background of low lifetime prevalence of illegal drug use in young people (<1%), early identification and engaging at-risk individuals for drug misuse and disorders intervention/treatment appear more critical. The present study aims to characterize the intervention history of healthcare and social care in the school attending illegal drugs-involved adolescents in Taiwan.
Methods: A retrospective cohort of 3836 students (aged 12-17) were identified from the 2012-2016 consultation and management databases, derived from a nationwide interventional program implemented by the Ministry of Education. Information concerning healthcare was retrieved from the 2009-2017 National Health Insurance Dataset, records of family-based social care were ascertained from the administrative data of national social welfare (i.e., poverty aid and child protection).
Results: Illegal drugs-involved middle- or high-school attending adolescents were 75% male and 33% under 15-year-old; 85% were engaged in ketamine—the gateway illegal drug in Taiwan. Nearly one half of adolescents came from the families near or below the poverty line, 6.44% and 8.50% had received child-protection and domestic violence intervention. Although 94% had utilized the outpatient services at least once in the year preceding the reporting by the schools, only 32 (0.8%) received the diagnosis code relevant to substance use and 6% have utilized mental health services. Within the year of intervention, 10% had dropped out of schools.
Conclusions: To mitigate the contributing factors underlying early-onset substance use and reduce the progression of substance use disorders in young people, the integrated intervention services with evidence-based strategies is urgently needed.
Financial Support: This study was supported by Ministry of Health and Welfare and National Health Research Institutes (Taiwan).

T11. Non-Engagement in Substance Use Treatment Among Women With Substance Use Disorders: A Latent Class Analysis on Multidimensional Barriers

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: While women with substance use disorders (SUDs) experience multifaceted and intersectional barriers in accessing substance use treatment (e.g., stigma, familial responsibilities), little is known about how these barriers may aggregate. Using a person-centered approach, this study evaluates patterns of treatment barriers and the factors associated with experiencing distinct sets of barriers to treatment among women with SUDs.
Methods: Data were from the NSDUH (2015-2019) among N=461 adult women with SUDs and no engagement in any form of substance use treatment in the past 12 months. We used latent class analysis (LCA) to examine 14 treatment barriers across multiple dimensions: logistics (e.g., transportation, childcare, convenience), stigma (negative perceptions from others and employment), and personal readiness (not ready to stop using drugs/not interested in treatment). Multinomial logistic regression assessed sociodemographic characteristics and types of SUDs on membership to barrier subgroups.
Results: Among the women, 36% were 18-25 years of age, 63% were Non-Hispanic White, and 35% had children. Most commonly reported SUDs were alcohol (43%), prescription drugs (23%, e.g., pain meds and psychotherapeutics), and methamphetamines (14%). Three classes were evident among our sample: lack of readiness to abstain from drug use (67%), logistical barriers and stigmatization (22%), and experiencing barriers across all dimensions (11%). Dependence on methamphetamines (aOR:2.56, p=0.03), having children (aOR:2.15, p=0.03), having more than a high school education (aOR:3.01, p=<0.01), and marriage (aOR:0.20, p=0.01) were significantly associated with belonging to the logistical barriers and stigmatization group, than to the lack of readiness group. Dependence on prescription drugs (aOR: 1.89, p=0.03) and having more than a high school education (aOR:2.28, p <0.01) were significant predictors of being in the all barriers group than to the lack of readiness group (aOR:2.28, p<0.01).
Conclusions: Drug preference and sociodemographic and family characteristics influence women's substance use treatment engagement and need further exploration.
Financial Support: K01DA051715 (PI: Jones, A.A.) PSU Prevention Research Center

T12. Non-Opioid Substance Use Among Patients Receiving Office-Based Buprenorphine Treatment

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Medications for opioid use disorder (MOUDs) are the gold standard for the treatment of opioid use disorder. However, there is much debate surrounding the need for adjunctive psychosocial support for individuals taking MOUDs. One factor that may impact the need for additional supports is whether the patient is using opioids exclusively or in addition to other non-opioid drugs as existing medications are not designed to impact non-opioid use. This study examined data from an ongoing trial to examine prevalence and patterns of non-opioid substance use among individuals who have recently initiated office-based buprenorphine treatment.
Methods: We examined urinalysis-confirmed substance use from a cohort of 68 male and female participants receiving office-based buprenorphine treatment at two federally qualified health centers in a large mid-Atlantic city. Participants enrolled into the larger study within one month of buprenorphine induction. At the time of enrollment, participants provided a urine specimen that was tested for 14 substances. Frequencies were calculated for the presence of each substance tested.
Results: Overall, 79% (n=54) of baseline urine screens were positive for at least one of the 14 substances tested. Non-opioid drugs were present in the large majority of urine specimens (71%; n = 48). Excluding marijuana from these figures, this percentage drops to 51% (n = 34). Marijuana (38%, n=26), cocaine (30%, n=21), and benzodiazepines (19%, n=13) were the most commonly detected non-opioid substances. Additionally, fentanyl was present in 34% (n=23) of the specimens.
Conclusions: These preliminary findings indicate that a substantial proportion of participants used other non-opioid substances following their induction onto buprenorphine. Because MOUDs are not designed to reduce non-opioid drug use, individuals who use multiple substances may require additional psychosocial supports. Future research is necessary to better understand when these supports are warranted and which may be most appropriate for whom.
Financial Support: Pennsylvania Department of Health (SAP#4100083338).

T13. One Person's Needs is Someone Else's Need Too: Attitudes Towards Harm Reduction and Low-Threshold Healthcare During COVID-19 Among People Who Use Drugs in Rural Southern Illinois

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To examine attitudes towards and utilization of harm reduction and healthcare services by people who use drugs (PWUD) in rural Illinois during COVID-19.
Methods: As part of an ongoing study of PWUD in rural Illinois, we conducted semi-structured qualitative interviews between June and November 2021. Interview topics were organized around the Consolidated Framework for Implementation Research (CFIR) to explore determinants related to accessing harm reduction services, with additional items surrounding the impacts of the COVID-19 pandemic on daily life, wellbeing, and drug use. We used a modified grounded theory approach to analyze participant responses.
Results: 20 participants (45% female, mean age of 38) completed interviews. With respect to overall wellbeing, the pandemic and practices including social distancing negatively influenced many interviewees' mental and emotional health; socioeconomic consequences of the pandemic often resulted in situations of financial or housing insecurity for interviewees, compounding the lower socioeconomic opportunity cited by PWUD living in this region. Most interviewees also noted the pandemic's impact on the drug supply, primarily regarding increased suspected fentanyl or other unwanted agents in drugs. Most interviewees had

not been vaccinated against COVID-19, citing distrust of the government and medical institutions as reasons for vaccine hesitancy. All but one interviewee (who was able to access all necessary medical services) endorsed interest in low-threshold healthcare should it be offered through a known local harm reduction agency, describing openness to learning about COVID-19 in this trusted setting, receiving services such as hepatitis C treatment and wound care, and participating in telehealth appointments from within the harm reduction organization's space.
Conclusions: The COVID-19 pandemic and its downstream effects increased risks experienced by rural PWUD. Integration of healthcare services into a harm reduction infrastructure may promote greater engagement with COVID-19 awareness and vaccination programs and other important healthcare services.
Financial Support: University of Chicago Pritzker School of Medicine

T14. Patients With a History of Foster Care Are at Higher Risk for Drug Overdose

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Foster care has been identified to impact lifetime mental health and substance use disorders negatively. While this link has been established in populations with mental health and substance use disorders separately, little is known about individuals who have co-occurring diagnoses of both (concurrent disorders). This study investigates whether individuals with a history of foster care (HoFC) have an increased risk for substance use overdose among patients with severe concurrent disorders.
Methods: 132 male and female inpatients with concurrent disorders completed a battery of self-report questionnaires. Drug use and overdose history were assessed using the Maudsley Addiction Profile and self-reported drug overdoses. Demographics and psychiatric diagnoses were retrieved through patient medical charts. Data were compared between individuals with and without HoFC.
Results: There were no differences in demographics or diagnoses between patients with (n=23; 29.3±10.5 years old, 11F) versus without HoFC (n=109; 39.0±11.4 years old, 36F). Patients with HoFC showed a greater likelihood of drug overdose (β=1.08, p=.04), fentanyl (β=1.19, p=.01), heroin (β=0.98, p=.04), and polysubstance use (β =1.18, p=.03), with no differential self-reported frequency of fentanyl or heroin use. Among those reporting ≥1x lifetime overdose, there was a pattern for patients with a HoFC of a greater number of stimulant overdoses relative to those without HoFC, but this effect was marginal (p=.057, BF01=0.38). No other differences were observed for opioids, alcohol, and benzodiazepines (BF01 ranged=0.92-3.97).
Conclusions: Findings suggest concurrent disorder patients with a HoFC are at higher risk for overdose, fentanyl, and heroin use. Further, we found evidence to suggest this increase in overdose risk may be more likely to involve stimulant use. The etiology of increased drug overdoses among individuals with a HoFC cannot be ascertained, given the cross-sectional nature of this study. Longitudinal studies investigating the potential problems contributing to stimulant use and other drugs linked to foster care are warranted.

T15. Prevalence of Substance Abuse Among Out-Of-School Youth in Motor Parks in Ikeja Local Government Area of Lagos State

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Substance abuse has been found to be on the increase among youth in Nigeria in recent times mainly due to the increased availability of these substances on Nigerian streets leading to health and social consequences. This study aimed at determining the prevalence of substance abuse among out-of-school youth in Ikeja Local Government Area of Lagos State.

Methods: This was a cross-sectional study conducted among out-of-school youths working as motor boys in Ikeja Local Government Area of Lagos State. We used a multi-stage sampling technique to select the participants and information was obtained using interviewer-administered questionnaires. Data was analyzed using Statistical Package for Social Science (SPSS) version 21 and knowledge scores were graded as "good", 'fair' and "poor" and practice was scored based on reports from the respondents.
Results: A total of 122 youth participated in this study who were all males. The mean age was 12.40 ± 1.32 years. Majority of respondents, 72 (59.0 %) had a poor knowledge of substance abuse. Increased frequency of substance abuse was associated with less education (OR = 1.51, 95% CI: 1.24–1.62) and being a product of a dysfunctional home (OR = 1.62, 95% CI: 1.31–1.73). Decreased frequency of abuse was associated with increasing age (OR = 0.22, 95% CI: 0.11–0.51) and regular attendance of a religious meetings (OR = 0.45, 95% CI:0.23–0.71) The most commonly used substances among the respondents were alcohol (31.3%), cigarette smoking (23.1%), marijuana (10.2%), codeine-containing cough syrups (7.4%) and tramadol (5.6%).
Conclusions: The study shows low level of knowledge and high prevalence of substance abuse in this group. Interventions should take into consideration the factors that have been found to increase the prevalence of abuse.

T16. The Association Between Socioeconomic Status, Delay Discounting, and Recovery From Substance Use Disorders

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: To examine the relationships between socioeconomic status (SES), domains of recovery (i.e., psychosocial functioning and relapse status), and CNDS functioning (as measured by delay discounting; DD) among individuals in recovery from substance use disorder (SUD).
Methods: Data (N=497) were collected from the International Quit and Recovery Registry (IQRR) to examine the association between objective SES (as measured by income and education), psychosocial functioning measures (e.g., the World Health Organization Quality of Life; WHO-QoL), and relapse status (i.e., the resurgence of DSM-5 SUD criteria in the last 3 months). A cross-sectional study design. Both sexes were included.
Results: A significant difference in WHO-QoL across the three SES levels (i.e., low, medium, high; Cohen's $f = 0.19$ to 0.43, all $ps<0.001$) among those with SUD was found. Specifically, those in the high SES level had significantly higher scores in the psychological, physical, and environmental domains compared to those in the low SES level. Interestingly, 40% of the current sample were in relapse status and SES levels were a significant predictor of SUD relapse/remission status ($p<0.001$) with a higher relapse rate among lower SES. In addition, the low SES group shows greater discounting of future rewards (higher impulsivity; Cohen's $f = 0.34$, all $p<0.001$). Moreover, significant negative relationships were found between DD and psychological, physical, and environmental domains of WHO-QoL (r ranges from -0.28 to -0.10, all $ps<0.02$).
Conclusions: The current findings indicate significant associations between SES, DD, and domains of recovery from SUD. This research may help identify subgroups that require unique interventions and special attention to overcome their addiction.
Financial Support: The Fralin Biomedical Research Institute at Virginia Tech Carilion

T17. "See The Need, Meet The Need:" Attitudes Toward Trauma-Informed Care Among Juvenile Justice Staff

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Criminal Justice
Abstract Detail Human

Abstract Category Original Research
Aim: Trauma and substance use (SU) are prevalent among youth within the juvenile justice (JJ) system. Trauma-informed care (TIC) is shown to reduce and prevent JJ-youth SU and increase staff compassion. As TIC can reduce SU, it is important to evaluate staff's attitudes toward TIC to effect change in JJ-youth SU. The present study examined possible predictors and attitudes toward TIC within JJ-facilities as part of an ongoing study on a trauma-informed intervention for JJ-youth and their caregivers.
Methods: A mixed-methods design used data from staff in three JJ-facilities with varying exposure to TIC (High, Medium, Low). Seventy-eight JJ-staff members participated in focus groups, and forty-five participated in the quantitative survey assessing attitudes toward TIC (Attitudes Related to Trauma-informed Care; ARTIC) and compassion fatigue and satisfaction (Professional Quality of Life; ProQol).
Results: JJ-staff expressed the utility and value of TIC in JJ-facilities, while acknowledging concerns. The facility with high TIC exposure reported more favorable attitudes regarding TIC than the medium and low facilities. Quantitative data corroborated these results indicating differences in ARTIC scores among the three facilities. In a linear regression, high exposure to TIC indicated more favorable attitudes toward TIC (M(SD) = 5.38 (.39)) than low (M(SD) = 4.83 (.71), $p = .04$) and medium (M(SD) = 4.64(.58), $p \leq .001$) facilities; however, the low and medium facilities' attitudes toward TIC did not differ. Furthermore, ARTIC scores were positively correlated with compassion satisfaction ($r = .33$, $p = .03$), and negatively correlated with burnout ($r = -.39$, $p = .009$) and secondary traumatic stress ($r = -.31$, $p = .05$).
Conclusions: Results demonstrate the acceptability of TIC in JJ-facilities, while illuminating staff concerns. Additionally, staff attitudes toward TIC are correlated with professional quality of life characteristics. Together, these results indicate that JJ-staff are open to using TIC to effect change in JJ-youth SU.
Financial Support: NIDA; Grant 1UH3DA050250, Danica Knight, Principal Investigator

T18. Addictive Characteristics of Patients With Cluster Headache

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Cluster headache (CH) is one of the most painful primitive headaches. Developments in neuroimaging have demonstrated activation of the ipsilateral hypothalamic and orexinergic systems, which is similar to findings in patients with addictions. Several studies have shown an association between CH and smoking. However, little data exists on the link between CH and other addictions, and impact of these addictions on clinical characteristics of the disease and efficacy of CH treatments.
The main objective of this study is to determine the association between different types of addictions (tobacco, alcohol, other substances, medications, gambling) and the clinical characteristics of CH (frequency, severity and duration of attacks) and the efficacy of acute and/or background CH treatments.
Methods (Optional): This is a prospective cohort study recruiting 150 patients with CH from the Pain Clinic, CHU of Bordeaux, France. To be included, patients have to be aged 18 or above, and fulfill the ICHD-III beta criteria for CH. Exclusion criteria are other primary headaches. Addictive characteristics and psychiatric comorbidities are evaluated with the ASI (addiction severity index) and the MINI (Mini International Neuropsychiatric Interview).
Conclusions: Expected results: This cohort study will, for the first time, describe the relationship between CH and addiction. If the study confirms an association, the first implication will be the need for a systematic exploration of addiction diagnosis in all patients consulting for a CH, in order to propose adequate management of the two disorders.
Financial Support: CHU de Bordeaux and Air Liquide Orkyn

T19. COVID-19 Vaccination Status and Concerns Among People Who Use Drugs in Oregon

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Drug Category Polydrug (i.e. concurrent use two or more drugs)

Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of this qualitative study was to examine COVID-19 vaccination acceptance and explore reasons for COVID-19 vaccine hesitancy among people who use drugs (PWUDs), a population with increased COVID-19 transmission and morbidity.
Methods: We conducted 34 in-depth semi-structured phone interviews with PWUDs in Oregon from May 11 to June 25, 2021. Eligible participants used illicit drugs in the past 30 days and were age 18 or greater. We used thematic analysis to analyze transcripts and construct themes.
Results: Most participants (71%) had not received the COVID-19 vaccine and were not planning on or were unsure about receiving it. Participants mistrusted the rapid vaccine development process and the agencies involved in the development (i.e., government and health care), reporting past negative experiences with these agencies and feeling these agencies were not helpful or may want to harm them. Participants shared varied and contrasting responses about who they would trust to provide information about the COVID-19 vaccine, including peer recovery support specialists (peers), doctors, or other health care professionals. When asked specifically about trusting peers, many participants believed peers to be honest and well-intentioned. Some participants shared they would be more likely to trust COVID-19 vaccine information from a peer if the peer partnered with someone in health care or "if they're a specialist in the medical field or part of the medical field". Participants noted they would be more likely to trust doctors or other health care professionals after more studies have been completed and the COVID-19 vaccine was FDA approved.
Conclusions: As addiction treatment and public health staff continue to respond to the evolving impacts of COVID-19, vaccination planning should be tailored to the unique needs of PWUD to increase COVID-19 vaccine acceptance in this high-risk population. Involving peers could help mitigate the effects of past stigmatizing experiences.
Financial Support: This work was supported by the National Institutes of Health, National Institute on Drug Abuse (UH3DA044831, UG1DA01581), Centers for Disease Control and Prevention (1 NU17CE925018-01-00), and the Oregon Clinical and Translational Research Institute (UL1TR002369).

T20. Determination of the Cause and the Manner of Death in Post-Mortem Cases in the West Bank in the Years 2011-2021: Mortality Related to Drugs and Toxic Substance Use in Post-Mortem Cases

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: A post-mortem examination is a reliable method to reveal possible hidden causes of death. However, due to the stigma associated with drug use, mortality data related to drug use is a neglected topic in local health in Palestine. We aimed to describe post-mortem examination cases' mortality data in general and, specifically, investigate the occurrence of death-related drug use in the West Bank in 2011-2021.
Methods: A retrospective study was conducted in the north of the West Bank. The total number of autopsied cases in the period from 2011 to 2021 was 673 cases.
Results: Natural death was the leading cause of death (40%), followed by homicide (30%), accident (17%), and suicide (12%). Homicide was more prevalent among males, with increased risk in young adults in the summer season. Moreover, Palestinian refugees were three times more likely to commit homicide than urban. Most suicide cases were males, and asphyxiation by hanging was the predominant cause. Children were five times, and young adults were nine times more likely to commit suicide than victims aged >40 years. In all mortality data related to intoxication, organophosphates were the leading cause of death in suicidal cases and multidrug misuse in unintentional death. Amphetamines were the most drugs found in combination with other drugs. Most of the deaths-related drug use were male prominent and from villages.
Conclusions: The increased rate of suicide and accidental death related to drug use, the age of victims, and the polydrug tested in these cases indicate that there is a hidden population of multidrug users in young adults and children. The type of combined drugs estimated the potential of the danger caused by these drugs.

Moreover, age-related increases in homicide and suicide rates highlight the vital role of raising national health awareness and improving the health care system in rural areas and refugee camps.

T21. Estimating the Impact of Stimulant Use on Initiation of Medication for Opioid Use Disorder Among Treatment-Seeking U.S. Adults

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Co-occurring stimulant use is widespread, increasing, and may present a significant challenge to treatment initiation among people with opioid use disorder (OUD). The aim of this study was to estimate the association between stimulant use and initiation of medication for OUD (MOUD) in two clinical trials and generalize findings to the U.S. adult population seeking OUD treatment.
Methods: Data from two National Drug Abuse Treatment Clinical Trials Network (CTN) trials (CTN 0051 and 0067) were harmonized and pooled. The association between time-varying stimulant use (methamphetamine, amphetamines, or cocaine) and time to first buprenorphine prescription or extended-release naltrexone injection was estimated using a Cox regression model adjusted for demographics, depression, alcohol use disorder, and time-varying opioid and benzodiazepine use. Then, inverse odds of selection weighting were used to generalize results to the U.S. adult treatment seeking population, as characterized by 2018-2019 National Survey on Drug Use and Health (NSDUH) respondents reporting receiving or seeking OUD treatment in the past year.
Results: Most trial participants (N = 684) were age 30-49 (50%), male (69%), and White (63%). In the trials, stimulant use was associated with a reduction in the likelihood of MOUD initiation by 36% (adjusted HR=0.64, 95% CI 0.45-0.91). Effects did not differ by type of stimulant, MOUD or by study. Trial participants were more likely to be male, nonwhite, unemployed, less educated, report recent injection drug use, and less likely to report a history of depression than NSDUH respondents. When associations were generalized to the U.S. adult treatment-seeking population, stimulant use was 10% more harmful than originally estimated in the trials, reducing the likelihood of treatment initiation by 46% (aHR=0.54, 95% CI 0.29-0.98).
Conclusions: Stimulant use is a barrier to MOUD initiation among people seeking treatment for OUD. Effects may be more pronounced in the "real-world" than suggested by clinical trials.
Financial Support: NIH/AHRQ K12 HS026370; NIDA UG1DA015815; NIDA UG1DA013035

T22. Feasibility of Using Social Media to Deliver an Evidence-Based HIV Prevention Intervention Among Rural Appalachian Women Who Use Drugs

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: Social media platforms are a viable means of delivering HIV prevention interventions. Given public health concerns around injection-related disease transmission in rural Appalachia, coupled with research suggesting the majority of women who use drugs in rural Appalachia use Facebook, this study aims to assess the feasibility of using Facebook for delivering an evidence-based HIV prevention intervention among a sample of high-risk, justice-involved rural Appalachian women who use drugs.
Methods: Sixty women from two rural Appalachian jails were randomly selected, screened, and interviewed. The NIDA Standard was adapted for this study for both content (tailored to rural Appalachian women) and context (delivery using Facebook). Women participated in the pilot intervention (known as Facebook NIDA Standard for Rural Appalachian Women – FB Standard RAW) for 12 weeks following

release from jail. Analyses were limited to 54 women who were released from jail during the study period and, thus, eligible for the intervention. Descriptive statistics about participant intervention initiation and engagement were used to assess feasibility and acceptability.
Results: More than two-thirds of participants (70.4%) accepted Facebook friend requests for the study site, and 72.2% interacted with staff through Facebook Messenger (average of 17.4 messages, SD=15.5). Sixty percent of the women in the FB Standard RAW intervention accepted the group invitation, viewing an average of 7 out of 14 available videos (SD=2.3). Participants also averaged more than 2 Facebook accounts (SD=1.9), which required additional effort by staff to make a connection following release from jail.
Conclusions: Results suggest that Facebook is a promising approach for increasing access to and engaging drug-using women in rural Appalachia in an online, cost-efficient HIV prevention intervention during community re-entry, and may signal implications for expanding the reach of HIV prevention services to other rural populations with limited access to traditional interventions.
Financial Support: Research was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number R34DA045563.

T23. Low Intensity Focused Ultrasound Targeting the Nucleus Accumbens as a Potential Adjunctive Treatment for Substance Use Disorder

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: To evaluate the safety, tolerability, feasibility and impact on substance craving of Low Intensity Focused Ultrasound (LIFU) as a neuromodulator for substance use disorder (SUD).
Methods: Individuals currently enrolled in a comprehensive SUD treatment program were eligible for the study. LIFU targeting the Nucleus Accumbens (NAc) was applied bilaterally. Participants received 20 minutes LIFU, first sham LIFU followed by 20 minutes of active LIFU. In addition to safety assessments completed 90 days post-LIFU, outcomes included the acute assessment of substance craving using a cue reactivity paradigm prior to, during, and following LIFU. Daily craving (non-cue induced) ratings, via a visual analog scale, were also assessed in the week prior to and the week following LIFU.
Results: Two participants (one male and one female, both in their early 30's), underwent LIFU targeting the NAc, which was safe and well-tolerated, during LIFU treatment as well as throughout the ninety day follow-up assessment. Relative to sham LIFU, active NAc LIFU acutely attenuated self-reported craving for all substances including opioids, alcohol, and benzodiazepines. In addition, relative to the week preceding LIFU treatment, daily craving ratings were significantly reduced for several substances during the week following NAc LIFU. Specifically, in the male participant, post-LIFU craving reductions were noted for opioids (3.6±0.5 vs. 1.8±0.5), alcohol (6.0±0.7 vs. 2.4±1.2), and benzodiazepines (2.8±0.4 vs. 0.0±0.0) and, in the female participant, post-LIFU reductions were noted for alcohol (3.0±1.5 vs. 0.0±0.0) and nicotine (5.6±1.9 vs. 1.2±0.8) (all p's <0.001).
Conclusions: LIFU targeting the NAc was safe and well-tolerated, acutely reduced cue-induced substance craving during the LIFU procedure, and potentially reduced craving in the week following LIFU treatment. While early observations are promising, NAc LIFU requires further investigation in a controlled trial to assess safety and therapeutic effect to elucidate the impact on substance craving and ultimately substance use and relapse.

T24. Methamphetamine Use and Risky Sex Among Justice-Involved Women With a History of Opioid Use Disorder (OUD)

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Drug Category Polydrug (i.e. concurrent use two or more drugs)

Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Women are the fastest growing segment of the criminal justice system, which has largely been attributed to the opioid epidemic. However, methamphetamine use has grown considerably among women, but less is known about justice-involved populations. This study proposes to: 1) profile methamphetamine use among justice-involved women with a history of OUD; 2) examine methamphetamine use as a correlate of high-risk sexual practices with male partners.
Methods: Baseline data was collected with incarcerated women (N=125) as part of the NIDA-funded Justice Community Opioid Innovation Network (JCOIN). Participants were randomly selected from jail rosters in six Kentucky facilities, screened for OUD history, and consented to participate. Analyses examined lifetime and recent meth use, risky sexual partners (injecting drugs or being incarcerated), transactional sex, and condom use.
Results: The majority reported methamphetamine use (95.2% lifetime, 82.4% recently during the 90 days prior to incarceration), and injection was the most common route of use (55.5%). Most reported having risky main partners (81.6% previously incarcerated, 56.0% injectors) and casual partners (56.8% previously incarcerated, 41.6% injectors). Most women (87%) also reported infrequent (never/sometimes) condom use and about half engaged in transactional sex (46.4%). Recent methamphetamine use was significantly associated with having a main male partner who injected drugs (60.2% vs. 36.4%, $p<.05$) and previous incarceration (85.4% vs. 63.6%, $p<.05$). Findings remained significant when controlling for demographics.
Conclusions: Findings suggest that methamphetamine use is common among justice-involved women with a history of OUD. Methamphetamine use was also associated with involvement with high-risk main male sexual partners, which may increase women's HIV risk as they transition to the community after jail release. Criminal justice venues (such as jails) may be ideal opportunities to provide outreach and intervention for HIV prevention and other risk reduction interventions among women who may not otherwise access services.
Financial Support: NIH/NIDA UG1DA050069; Staton PI

T25. Model-Based Decision Making is Related to Reflection Impulsivity: Findings From Exploratory Correlational Analyses Between Computational and Traditional Impulsivity Outcomes

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: Impulsive decision making is a well-established risk for drug use. Recent advances in computational modeling have identified distinct cognitive processes involved in impulsive decision making; however, little is known of the relationships between computational derived and traditional measures of impulsivity. We present findings from exploratory correlational analyses between model-based decision making and traditional impulsivity outcomes in substance use disorder (SUD) inpatients and healthy controls.
Methods: 45 patients (38.5±11.5 years, 14F) and 50 healthy controls (30.9±10.0 years, 25F) completed a battery of impulsivity self-reports and behavioral tasks, including the Cambridge Gambling Task (CGT) and Informational Sampling Task (IST), assessing risky decision making and reflection impulsivity, respectively. CGT data were used to generate computational outcomes (Probability Distortion, Loss Sensitivity, Delay Discounting, Choice Consistency) based on the Cumulative Model. IST comprised decreasing-/fixed-win conditions, where there was cost/no cost for obtaining information relevant to optimizing reward outcomes.
Results: In controls, Probability Distortion ($r=.38$, $p=.009$) and Choice Consistency ($r=.35$, $p=.02$) were positively correlated with amount of information sampled under fixed-win condition, and Loss Sensitivity was positively correlated with amount of information sampling ($r=.34$,$p=.02$). All computational outcomes, except Choice Consistency, were correlated with ≥1 self-report composite score (r's ranged $|.40|$ to $|.52|$, p's$<.05$), with no other correlations across impulsivity measures in controls. In patients, no correlations between computational and traditional impulsivity measures were statistically significant.

Conclusions: Findings indicate model-based impulsive decision making outcomes are associated with aspects of reflection impulsivity. Patterns of relationships suggest individual model-assessed decisional processes may be reflective of the tradeoff between utility of information and its cost. It is worth considering that the absence of such patterns in patients might contribute to decision making leading to suboptimal outcomes. We present exploratory data to stimulate future work into relating model-based (e.g. habitual) and model-free (e.g. reflective) decision making.
Financial Support: British Columbia Provincial Health Services Authority

T26. Predictors of Post Release Service Utilization Among the Formerly Incarcerated With Substance Use Disorders

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: This abstract examines how substance abuse prison treatment and social support relationship type influence post-release service utilization across nine different service domains among formerly incarcerated men and women with substance use disorders (SUDs). Perceived Service needs is also explored as a mediator.
Methods: Data for this study was from the Multi-site Randomized Controlled Trial of the 5-Key Model for Reentry Data. This longitudinal data focuses on men and women recently release from prison across four states (FL, KY, PA, and TX) and followed them from incarceration through up to 15 months post-release (5 timepoints). Multilevel logistic regression was utilized to examine predictors of post-release service utilization among men and women in the control arm of the study diagnosed with SUDs prior to their release from prison (N=504).
Results: Results indicate statistically significant ($p<.05$) post-release service utilization models across 9 service domains (i.e. substance abuse; mental health; life skills; relationship; health; job readiness; education; housing; cognitive), with a heavy emphasis on the strength of perceived need. There were statistically significant relationship observed among the independent variables, prison substance abuse treatment and relationship type of social support. Additionally, consistent statistically significant differences among race/ethnicity for post-release education services were found ($p<.05$).
Conclusions: Differences in statistically significant covariates specific to various service domains will be discussed speaking to the importance of integrated and individualized care for individuals reentering the community from prison with SUDs. Implications for prison treatment and service delivery systems will also be discussed.
Financial Support: NIDA T32DA01035 (PI: Cunninghham-Williams and Bucholz)

T27. Prevalence of Comorbid Health Diagnoses by Body Systems of Persons Presenting in Texas Hospitals With a Substance Use Diagnosis

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Project HOMES is a longitudinal evaluation study of level II and III recovery residences that examines (a) resident-level outcomes, (b) cost-effectiveness, and (c) healthcare utilization. To begin examining the effect of living in a recovery residence on healthcare utilization, data from the 2018-2020 Texas Health Care

Information Collection (THCIC) were examined. The THCIC dataset includes emergency department (ED) and inpatient discharge data for the State of Texas.
Methods: International Classification of Disease codes (ICD-10) were used to identify emergency and inpatient admissions with a primary and/or secondary diagnosis of substance use in Texas during 2018 (N= 3,020,103), 2019 (N= 3,078,411), and 2020 (N= 2,713,035). These admissions were categorized by substance and body system. Descriptive and bivariate data of those body systems with the highest proportion of diagnoses were reported by substance.
Results: Across years, the majority of patients with a primary substance use diagnosis were 18-44 years of age (45.93%) or 45-64 years of age (25.46%). Approximately half were male (51.43%), non-Hispanic White (50.85%), and uninsured (47.62%). The greatest proportion of ED and inpatient admissions across years were for alcohol (42.98% ED; 62.01% inpatient) and stimulants (27.53% ED; 14.71% inpatient); opioids accounted for 7.09% of ED and 9.33% inpatient admissions. For all admissions across years, the most common secondary body system diagnoses were for mental/behavioral health (20.08%) followed by endocrine/metabolic (8.46%), circulatory (7.71%), nervous (5.59%), respiratory (4.88%), genitourinary (3.29%), musculoskeletal (3.07%), digestive (3.05%), blood (2.59%), integumentary (0.74%), and visual (0.59%). Additional bivariate analyses are presented.
Conclusions: In addition to partnering with hospital systems to ensure the implementation of brief interventions for persons presenting with comorbid health conditions, these data provide persons working in substance use recovery with insights into comorbid health conditions most likely to be affecting the health of current or future clients of recovery support services.
Financial Support: This project is supported by the Texas Health and Human Services Commission with zero percentage financed by non-governmental sources (contract number HHS000563200001). The contents are those of the presenter(s) and do not necessarily represent the official views of, nor an endorsement by HHSC or the Texas government.

T28. Serious Psychological Distress, Substance Use Disorders, and the COVID-19 Pandemic: An Examination of Multiple Mental Health and Social Issues Among Men and Women in the United States in 2020

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: While the Covid-19 pandemic increased social isolation and economic challenges, these adverse effects on distress levels of individuals with substance use disorders (SUDs) warrant exploration in a nationally representative sample. As such, this study assesses the association between SUD, economic hardship, and related risk and protective factors on serious psychological distress (SPD) during the COVID-19 pandemic.
Methods: Data were from the NSDUH (2020) among N= 25,746, representing 238,677,123 US adults. SPD was classified as scoring a 13 or more on the Kessler (K6) distress scale. SUDs were determined using DSM5 criteria. Logistic regressions evaluated the association between sex/gender, protective (social support, religion), and risk (SUD, poverty) factors on SPD.
Results: Our sample was 51% female, 63% self-identified as Non-Hispanic White, 14% lived below the poverty threshold, 15% reported SUDs, and 10% reported SPD. After controlling for socio-demographic and related factors of SPD, having a SUD was the strongest correlate of SPD, with individuals with SUDs nearly four times more likely to report SPD (aOR=3.57, 95% CI=2.94, 4.33). Other significant correlates of SPD included: female sex (aOR=1.65 95% CI= .41, 1.97), having an income level at or below the federal poverty threshold (aOR=1.68, 95% C =1.33, 2.13) or two times the poverty threshold (aOR=1.26, 95% CI=1.01, 1.57), and higher levels of religiosity (aOR=0.74, 95% CI=0.61, 0.89). Sex stratified regressions illustrated that religiosity, self-identifying as Black, and high levels of education were protective against SPD for females but not males. In contrast, poverty level was more associated with SPD in females than males.
Conclusions: In the United States, individuals with SUDs were nearly four times more likely to report SPD than those without SUDs, controlling for economic hardship and markers of social support during the pandemic year of 2020. Effective interventions to reduce SPD among individuals with SUDs are needed.

Financial Support: K01DA051715 (PI: Jones, A.A.)

T29. Sex Differences in Neural Responses to Stress and Drug Cues is Predictive of Future Substance Use Disorder Relapse Severity

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Substance used disorders (SUD) are chronic relapsing illness; stress and/or drug/alcohol-related cues significantly increase drug craving and relapse risk, but neural mechanisms that increase such risk are not clear and sex differences in these relationships have not been examined thus far. To examine neural and behavioral responses to stress and drug cue provocation and prospectively assess relapse outcomes in men and women with SUD.
Methods: Abstinent, inpatient treatment engaged men (N=46) and women (N=26) with SUD were enrolled and followed post-treatment for a 90-day period to assess relapse. Functional magnetic resonance imaging (FMRI) experiment with randomized exposure to individualized script-driven imagery trials of stress, drug/alcohol cues, and neutral-relaxing scenarios in 6 separate blocks, followed by a prospective longitudinal observational design to assess substance use in the 90 days after discharge from inpatient treatment.
Results: Both SUD men and women reported increased anxiety (S>N: P=<.001; D>N: P=<.001), heart rate (S>N: P=<.001; D>N: P=.004), and craving (S>N: P=<.001; D>N: P=<.001) in response to stress and drug/alcohol-related cues compared to neutral-relaxing cues. After inpatient treatment, women had significantly (P=.006) more days of substance use (44.61 days) compared to men (18.43 days). Hyperactivation in the caudate and putamen during drug/alcohol cue trials significantly predicted greater follow-up days of substance use in men, while hypoactivation in the right insula and left dorsolateral prefrontal cortex (DLPFC) during drug/alcohol cue trials and hypoactivation in the ventromedial prefrontal cortex (vmPFC) during stress cue trials significantly predicted higher subsequent days of substance use in women (FWE whole brain corrected at p=.05).
Conclusions: Findings indicate significant sex-specific functional brain responses to stress and drug-related cues that are associated with future drug use outcomes post inpatient treatment. These results suggest the need to develop sex-specific treatments to improve SUD treatment outcomes in men and women.
Financial Support: Supported by NIH Grants, P50-DA016556, R01-AA013892, 5T32DA022975-12

T30. Sex Work and Overdose Risk Among Women Who Use Drugs in Vancouver, Canada

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Although women who use drugs and engage in sex work experience heightened drug-related health inequities, such as HIV, comparatively little is known about their overdose risk. Therefore, we examined the association between sex work and non-fatal overdose among women who use drugs in Vancouver, Canada, between 2005 – 2018.
Methods: Data were derived from two prospective cohort studies, the AIDS Care Cohort to Evaluate Exposure to Survival Services and Vancouver Injection Drug Users Study. Sex work was defined as trading sex for money, goods, or services in the six months preceding each study interview. We used univariate and multivariate generalized estimating equations (GEE) to evaluate the association between sex work and non-fatal overdose. The following individual and structural covariates were included in the multivariate GEE: baseline minority sexual orientation (lesbian, gay, bisexual, or queer) and time-updated age, homelessness,

heroin, alcohol, and stimulant use, incarceration, experiences of sexual or physical violence, safe consumption site utilization, and calendar year.
Results: Between 2005 – 2018, a total of 27,635 visits were completed by 2,350 cis- and transgender women. Women reported overdoses in 1816 (7%) visits. At baseline, 12% versus 9% of women who did sex work compared to those that did not reported overdose in the preceding six months. In the unadjusted GEE, women who did sex work experienced a 1.62 (95% CI: 1.37- 1.93) times increased risk of overdose. However, in the multivariable GEE (adjusted for individual and structural covariates) the sex work association with overdose was attenuated and not significant (aOR: 1.09; 95% CI: 0.92–1.30).
Conclusions: While women who use drugs and engage in sex work face an elevated burden of overdose, further research is needed to clarify the most salient individual and structural factors, rather than sex work itself, that explain the elevated risk to guide targeted overdose prevention interventions.

T31. Suicidal Ideation, Planning, and Attempts in Adolescents and Adults During the COVID-19 Pandemic: The Role of Substance Use Disorders and Sex/Gender

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The COVID-19 pandemic has been linked with increased distress stemming from the disruption of perceived stability. However, few nationally representative studies exist examining suicidality during the pandemic, particularly among those with substance use disorders (SUDs). We explore the role of SUDs on suicidality among adults and adolescents in 2020.
Methods: Data were derived from N=26,207 participants, representing 240 million adults weighted, and N=5,723, representing 25 million adolescents (12-17yrs.) who completed the NSDUH (2020. Separate logistic regressions for adults and adolescents were used to assess the association of DSM-5 SUDs, related factors, and suicidality (ideation, planning, and attempts).
Results: In 2020, around 12 million US adults (5%) and 3.3 million (13%) adolescents seriously contemplated suicide, 3 million adults (1.5%) and 1.2 million (6%) adolescents made a suicide plan, and 1.1 million adults (0.5%) and 1 million adolescents (4%) attempted suicide. Adults with SUDs were nearly four times more likely to seriously consider suicide (aOR=3.94, 95%CI: 3.19, 4.86), three times more likely to make a suicide plan (aOR=3.09, 95%CI: 2.25, 4.25), and nearly four times more likely to attempt suicide (aOR=3.77, 95%CI: 2.30, 6.19) than adults without SUDs. Adolescents with SUDs were four times more likely to consider suicide (aOR=3.94, 95%CI: 3.19, 4.86); however, they were five times as likely to make a suicide plan (aOR=5.14, 95%CI: 3.25, 8.13) and to attempt suicide (aOR=5.27, 95%CI: 2.91, 9.53) than adolescents without SUDs. Adult females and individuals experiencing poverty were twice as likely to attempt suicide than others. Adolescent females were 3-5 times more likely to seriously consider, plan, and attempt suicides than males.
Conclusions: Individuals with SUDs were significantly more likely to consider, plan, and attempt suicide than those without SUDs in 2020, with this association even more pronounced among adolescents. Interventions to curb suicidality among individuals with SUDs are crucial.
Financial Support: K01DA051715 (PI: Jones, A.A.)

T32. Survey of Substance Use and Characteristics Associated to Problematic Use in a French Community Structure for People With Mental Disorders

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: To describe substance use and to screen for problematic use (and associated factors), among adult workers with mental handicap engaged in a French Help center through work structure.

Methods: This was a cross-sectional survey conducted in Spring 2021. We used an anonymous self-administered questionnaire to assess use of tobacco, alcohol, psychotropic drugs, opiates and other illegal substances. Problematic use was assessed with an adaption of the CAGE. Questionnaire gathered data on age, gender, education, type of handicap, autonomy, substance use motivations. Study was proposed to all adults working in the center, except when mental handicap or behavioral disorders were too severe to be compatible with the survey. After presentation, the questionnaire was self-administered by volunteers during an individual appointment with an on-site trained and trusted nurse proposing help to ensure comprehension, when subjects asked for it, with non-judgmental attitude. All data were confidential and analyzed anonymously.
Results: Response rate was 86.3% (sample size n=282 /328). Prevalences of current use were 59.2% (alcohol), 31.9% (tobacco), 18.2% (cocaine, stimulant), 9.9% (psychotropic drugs) or lower (others), essentially for recreational purpose or to alleviate a tension. Tobacco and cannabis were the most reported for daily use (72.1% and 55.6% of current users). A third of our sample (31.6% n=89) was screened with a least one current problematic use, mostly tobacco (27.7%) and alcohol (11.0%). Factors associated with problematic use were being male, learning disability, higher autonomy (autonomous housing vs. parental or institutional housing), and higher education (having at least 1 diploma vs. none), $p<0.01$.
Conclusions: Despite the protective context of the institution, people with mental handicap met problematic substances uses in our sample. Our survey showed several associated factors that could help detection. Interestingly, these included autonomy and cognitive efficiency, which facilitates access to use.

T33. Adolescent Behavioral Responses to COVID-19 and the Development of the Pandemic Response Index

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: This study examines the relationship between COVID-19 pandemic-related lockdowns and substance use behaviors among a sample of adolescent primary care patients.
Methods: Data were derived from a stepped-wedge randomized trial of screening, brief intervention, and referral to treatment (SBIRT) among adolescents (aged 12-17, inclusive). A subset of participants (N=249) completed a 12-month follow-up survey that also included a questionnaire developed from the CDC COVID-19 “At Risk Populations” survey bank. These items were analyzed as five distinct indices, together referred to as the Pandemic Response Indices (PRI): Positive Actions (range 1-6; M 3.78; SD 1.49), Negative Actions (range 1-3; M 1.18; SD 0.92), Anti-Social Behavior (range 1-8; M 2.99; SD 1.87), Family Conflict (range 1-4; M 0.84; SD 1.04), and Family Stress (range 1-4; M 0.38; SD 0.82). Participants’ substance use behaviors were assessed with the ASSIST. Separate logistic regression analyses were conducted for past 30-day: tobacco, alcohol, marijuana, and any substance use.
Results: The sample was primarily white (70%), non-Hispanic (63%), with an average age of 14.2 (1.8) years. Significant findings in regard to the PRI were: the odds of tobacco use decreased 50% with each 1 SD increase in Positive Action score ($p<.001$), and increased 82% with each 1 SD increase in Family Stress score ($p=.002$); the odds of alcohol use increased 60% with each 1 SD increase in Negative Actions score ($p=.026$), and increased 67% with each 1 SD increase in Antisocial Behavior score ($p=.011$); and, the odds of any substance use increased 45% with each 1 SD increase in Family Stress score ($p=.004$). There were no significant PRI associations specific to marijuana use.
Conclusions: Several indices linked to pandemic experiences were significantly associated with adolescent substance use behaviors during COVID-19 lockdown.
Financial Support: Conrad N. Hilton Foundation (Grant number 16743).

T34. An Evaluation of Change in Coping Skills From Clinician- Versus Computer-Delivered CBT

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Drug Category Polydrug (i.e. concurrent use two or more drugs)

Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Cognitive behavioral therapy (CBT) is an evidence-based treatment for substance use disorders that is purported to work by improving individuals' coping skills. However, there is limited understanding of how CBT's mechanisms of action might differ when delivered through a computer program. This study will fill this gap by examining change in coping skills acquired during and after treatment using data from a completed randomized clinical trial testing the efficacy of a computerized cognitive behavioral therapy program (CBT4CBT; Kiluk et al., 2018).
Methods: Participants in the trial were 137 individuals (75% male; 49% Black, 34% Caucasian) seeking services at an outpatient substance use treatment center. Assessments occurred before treatment, mid-treatment, at the 12-week treatment termination point, and after termination. Change in the quantity and quality of coping skills were compared across the following treatment conditions: treatment as usual (TAU); clinician-delivered CBT; and CBT4CBT. We hypothesized the CBT4CBT group would experience the largest increases in coping skill quality and quantity.
Results: Descriptive analyses demonstrated increases in mean scores of coping skill quality in the CBT (pre-treatment M = 4.09; treatment termination M = 4.37; follow-up M = 4.59), TAU (pre-treatment M = 4.11; treatment termination M = 4.50; follow-up M = 4.62), and CBT4CBT (pre-treatment M = 4.19; treatment termination M = 4.76; follow-up M = 4.63) groups at the treatment termination point. Additional analyses will include random effects regressions with planned contrasts to examine change in quantity and quality of coping skills within treatment and through follow-up.
Conclusions: Results will advance the literature on mediators of computer-delivered CBT for substance use disorders as well as provide novel data regarding differences in coping skill acquisition across CBT delivery methods.
Financial Support: Supported by grants R37-DA015969 and P50-DA09241 from NIDA and grant R01-AA024122 from NIAAA.

T35. Association of Unhealthy Alcohol and Drug Use With Healthcare Utilization Among Adult Primary Care Patients

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Patients with substance use disorders are disproportionately represented in medical acute care settings, but less is known about how frequency of healthcare utilization relates to primary care patients' substance use. As a part of an implementation study of electronic health record (EHR)-integrated substance use screening in primary care, conducted in the NIDA Clinical Trials Network, we sought to understand the relationship between healthcare utilization and unhealthy alcohol and drug use.
Methods: Patient-level data were collected from 6 primary care clinics in the year of, and year prior to, implementation of clinic-wide universal screening for alcohol and drugs. EHR Screening and assessment results identified moderate-high risk use of alcohol (AUDIT-C score > 4(men), >3(women)) and drugs (DAST-10 score >3). Logistic regression models were used to examine the relationship between substance use risk and number of past year primary care (PC), emergency department (ED) and hospital visits.
Results: Of the 92,535 patients with primary care visits, 72% were screened. Among those screened positive (alcohol n= 26515; drugs n= 1965), 46% had moderate-high risk alcohol use, and 15% had moderate-high risk drug use. Controlling for key demographics, patients with greater healthcare utilization were more likely to have moderate-high risk alcohol use. This relationship was seen for PC (O.R.: 1.15; 95% CI: 1.03-1:19), ED (O.R.: 1.20; 95% CI:1.07-1.35), and hospital (O.R.: 1.78; 95% CI: 1.52-2.09)

utilization. No significant association was seen between healthcare utilization and moderate-high risk drug use.
Conclusions: Greater healthcare utilization was associated with higher likelihood of having moderate-high risk alcohol use. Although guidelines recommend screening all adult primary care patients for alcohol and drug use, our findings suggest that patients with high frequency healthcare utilization could be prioritized for alcohol screening. The lack of association between healthcare utilization and drug use may be related to lower rates of patients screening positive for drug use.
Financial Support: Supported by National Institute on Drug Abuse cooperative awards: U10DA013035, UG1DA013035, and UG1DA015831

T36. Causal Relationships Between High Levels of Substance Use, Emotions, and Social Support

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Our aim in this study is to use data-driven methods to describe how social and emotional factors are linked to high levels of substance use. We hypothesized that social-emotional factors interact to causally drive substance use.
Methods: We used Causal Discovery Analysis (CDA) with data from a community data set of young adults, the Human Connectome Project (N=1192, age: 22-35, 54% female). We included all available data on social and emotional function (NIH toolbox), as well as indicators of substance use levels (alcohol, tobacco, cannabis, illicit drug use). The data-driven CDA algorithm (Greedy Fast Causal Inference) generated an integrated causal model relating all of these factors.
Results: The model produced by CDA found that high levels of aggressive behaviors and having more friends were causally linked to higher levels of legal drug use. High levels of legal drug use in turn caused high levels of illegal drug use. Negative social-emotional factors such as stress, sadness, fear, perceived negative social relationships and loneliness caused substance use indirectly, by influencing both anger/aggression and friendships. Higher positive affect and life satisfaction had a buffer function, being causally linked to lower substance use levels.
Conclusions: Our findings suggest that a complex interplay between social-emotional factors drives high substance use levels, demonstrating a crucial and underappreciated role of social behaviors. Research into the importance of social behavior as a maintenance mechanism in substance use disorder has only recently received more attention. Our findings from a large sample of young adults illustrate the importance of this research and the need to better understand the complex social-emotional dynamics underlying substance abuse.
Financial Support: National Institute of Neurological Disorders and Stroke T32NS105604-04

T37. Distinguishing Differences in Polysubstance Use by Sex Among Persons Who Use Cocaine

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: To better understand polysubstance use variation among people who use cocaine.
Methods: People with past 30 days use of cocaine (n=148) were interviewed with the Substance Abuse Module (SAM) to assess criteria for past 12-month SUDs and the Polysubstance Substance Use-Temporal Patterns Section (PSU-TPS) to determine past 30-day use of cocaine, alcohol, and marijuana.
Results: Men 58.1%
Women 41.9%

Men with cocaine use disorder (CUD) (n=38; 25.7%) reported the highest average number of days of alcohol (12.9 days) and marijuana (16.4 days) use in the past 30 days compared to women with CUD (n=35; 23.6%), who reported an average of 8.8 days of alcohol and 15.40 days of marijuana use. Men without CUD (n=48; 32.5%) reported 11.1 days of alcohol and 11.5 days of marijuana use compared to women without CUD (n=27; 18.2%), who reported an average of 8.4 days of alcohol and an average of 17.7 days of marijuana use. No statistically significant difference in mean days of alcohol or marijuana use was found by sex among people with and without CUD.
Conclusions: Men with CUD appeared to have a higher average of reported alcohol and marijuana days than men without CUD, women with CUD, and women without CUD but due to a small sample size, these differences did not reach a statistically significant level.
Financial Support: The Identifying Patterns of Human Polysubstance Use to Guide Development of Rodent Models Study was supported by the National Institute on Drug Abuse (NIDA) R21/R33DA045140 (PI: Knackstedt and Cottler) and T32DA035167 (PI: Cottler).

T38. Gender Differences in Substance Use, Eating, and Other Addictive Behaviors Among Bariatric Surgery Patients

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: While bariatric (weight loss) surgery patients have been identified as at risk for other addictive behaviors, little is known about their alcohol and other drug use pre- and post-surgery. The present study examines prevalence rates of substance use and related problems and other addictive behaviors in a sample of bariatric surgery patients.
Methods: Participants are bariatric surgery patients recruited through social media and ResearchMatch.org who complete an online survey comparing pre- and post-surgery measures of substance use and other addictive behaviors. Additional questions assess their perceptions surrounding substance use problems both before and after surgery. Preliminary data are summarized below.
Results: Pilot sample (N=24) was 83.3% female, 12.5% male, and 4.2% Gender Variant/Non-Conforming; 95.8% of participants identified as white. 95.8% screened positive for problematic binge eating behaviors. One-third (34.8%) reported it occurred only before surgery while the other 65.2% said it was present both before and after surgery. Almost two-thirds (62.3%) of participants reported problematic restrictive eating behaviors with 69.2% of them stating it was present both pre- and post-surgery. Among alcohol drinkers (88%), participants reported heaviest pre-surgery drinking of 8.6 drinking days per month (range 1-30) as compared to 5.6 drinking days post-surgery (range 1-30). 20.9% screened at risk for alcohol problems (CAGE score of ≥2).37.5% of the sample reported smoking > 100 cigarettes in their lifetime and one-third (33.3%) reported never having tried a cigarette. Nearly 2/3 participants reported using at least one drug 6+ times (lifetime). Most participants (64%) reported only marijuana use. 8.3% reported an increase in substance use and 8.3% reported their use decreased during this time.
Conclusions: Study recruitment will end in Spring 2022 (planned N=200), allowing for analyses of substance use and related problems by sex/gender. Preliminary analysis found changes in eating, alcohol, and drug use pre- to post-surgery. behaviors and substance use pre- to post-surgery.

T39. Incarcerated Individuals With Co-Occurring Stimulant and Opioid Use Disorder in Rural Massachusetts: Needs and Use of Medications to Treat Opioid Use Disorder

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research

Aim: Co-occurring stimulant and opioid use are known to increase risks for overdose and incarceration, but little is known about this population's health needs and use of health services while incarcerated.
Methods: We examined the characteristics and use of health services among adults with opioid use disorder incarcerated in two rural Massachusetts jails (n=347) who did (n=175) and did not have a co-occurring stimulant use disorder (n=172). The primary outcome was in-jail prescription of medications to treat opioid use disorder (MOUD). Using logistic regression, we investigated co-occurring stimulant and opioid use as a predictor, controlling for covariates.
Results: Compared to individuals with only an opioid use disorder, more individuals with a co-occurring stimulant and opioid use disorder reported injection drug use (53.1% vs. 34.9%, $p<0.001$) and opioid use (74.3% vs. 55.8%, $p<0.001$) in the 30-days prior to incarceration; fewer were employed (6.3% vs. 25.6%, $p<0.001$) and fewer reported receipt of prescribed psychological medication (30.3% vs. 40.7%, $p<0.05$). A similar proportion of each group (about 50%) received MOUD while incarcerated, however more individuals with co-occurring stimulant and opioid use disorder were prescribed methadone (66.7% vs. 33.3%) and fewer received buprenorphine (40.3% vs. 59.7%). Individuals with co-occurring stimulant and opioid use disorder were less likely to receive MOUD than individuals with only opioid use disorder (odds ratio 0.34, 95% confidence interval 0.16, 0.73), net of covariates. The likelihood that individuals with co-occurring stimulant and opioid use disorder received MOUD while incarcerated was moderated by site, underscoring differences by site in policies and practices that determine receipt of MOUD.
Conclusions: Incarcerated individuals with co-occurring stimulant and opioid use disorder have complex health needs, and they are less likely to be prescribed MOUD while incarcerated. Understanding individual and contextual factors related to this population's use of MOUD may aid efforts to optimize care during incarceration and community re-entry.
Financial Support: This work was supported by the Substance Abuse and Mental Health Services Administration (SAMHSA) (1H79TI081387-01).

T40. Treatment Retention, Return to Use, and Recovery Support Following Post-COVID-19 Relaxation of Methadone Take-Home Dosing in Two Rural Opioid Treatment Programs: A Mixed Methods Analysis

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: In March 2020, the Substance Abuse and Mental Health Services Administration permitted Opioid Treatment Programs (OTPs) to relax restrictions on take-home methadone and promoted telehealth to minimize potential exposures to COVID-19. We assessed the effects of COVID-19-related changes in take-home methadone dosing in two OTPs serving five rural Oregon counties.
Methods: We used a mixed-methods convergent design. We extracted urine drug toxicology (UDT) results, take-home methadone regimens, and treatment retention from electronic health records (EHR). We used a mixed-effects negative binomial regression model to determine patient-level differences in take-home doses before and after COVID-19-related policy changes and their impact on treatment discontinuation, and UDT positivity. Semi-structured qualitative interviews (n=32) explored patient reactions to increased take-home dosing and reduced clinic visits to provide context for quantitative findings.
Results: Of the 391 patients, the number of take-home doses increased in the post-COVID-19 period for patients engaged in treatment for more than 180 days (Median: 8 vs 13 take-home doses per month, $p = 0.011$). Take-homes did not increase for patients with fewer days of treatment. Each percentage point increase in take-home dosing above what would be expected without COVID-19 policy changes was negatively associated with the percent of UDT positive for opioids ($B = -0.12$, CI [-0.21, -0.04], $p = 0.005$) and the probability of treatment discontinuation ($aOR = 0.97$, CI [0.95, 0.99], $p = 0.003$). Qualitative analysis revealed three themes explaining how increased take-home dosing supported recovery: 1) value of feeling trusted with increased responsibility; 2) reduced travel time permitted increased employment and recreation; and 3) reduced exposure to individuals less stable in recovery and potential triggers.

Conclusions: Take-home methadone dose relaxations were associated with increased methadone take-home doses, improved retention, and decreased UDT opioid positive results. Qualitative findings of enhanced recovery suggest feasibility and desirability of fewer take-home restrictions without safety harms.
Financial Support: National Institute on Drug Abuse awards 3UH3DA044831-03S1; AHRQ K12 HS026370

T41. Patterns of Past-Month and Lifetime Polysubstance Use are Associated With Co-Occurring Psychosocial Stress, Co-Cooccurring Psychiatric Disorders, and Overdose in Persons Seeking Treatment for Substance Use Disorders

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Given the sequelae associated with polysubstance use, individuals seeking treatment for the use of multiple substances may exhibit greater clinical complexity than persons using single substances. We examined patterns of polysubstance use among individuals entering treatment, as well as clinical correlates that may be the target of interventions.
Methods: Participants (N=28,526) were drawn from a dataset of individuals who presented for admission to addiction treatment facilities in the United States. Participants reported on their past month and lifetime substance use of thirteen substances. A 3-step latent class analysis (LCA) was used to examine a number of potential correlates between class membership and demographic risk factors (age, gender); psychosocial stress (unstable housing status, unemployment), co-occurring psychiatric disorders (depression, generalized anxiety disorder, PTSD), and other clinically-relevant phenomena (recent self-harm, overdose).
Results: A seven-class model best fit the data: 1) Alcohol primary, Low lifetime substance use, and 2) Moderate probability of past month alcohol, marijuana, and/or opioid use; Low lifetime substance use. 3) Alcohol primary, Lifetime marijuana and cocaine use. 4) Opioid/heroin primary, Lifetime use of hallucinogens, club drugs, amphetamines, and cocaine, 5) Moderate probability of past-month alcohol, marijuana, and/or opioid use; Lifetime use of various substances; 6) Alcohol and cannabis primary; Lifetime use of various substances; and 7) High past-month polysubstance use. Membership in the latter six latent classes relative to class 1 was predicted by younger age, male gender, unemployment, unstable living status, and screening positive for depression. Individuals in class 7 (high past month polysubstance use) were the most likely to screen positive for depression, PTSD, and recent overdose.
Conclusions: Individuals with greater polysubstance use present to treatment with significant clinical complexity across a number of domains. We recommend integrated and tailored treatment that focuses on specific subgroups at risk for polysubstance use, as well as reducing related harms.
Financial Support: T32DA007209 (Bigelow)

T42. Perceived Impact of COVID-19 on Substance Use and Mental Health in People Who Use Opioids (PWUO) in Syringe Services Programs (SSPs) in Southeast U.S. Cities

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid-related overdoses skyrocketed during the COVID-19 pandemic, with noticeable decline in service access. Given marked increases in other substance use and psychological distress (anxiety, depression) among vulnerable populations that can lead to HIV risk behavior, this study examined the

perceived COVID-19 impact on substance use and mental health in people who use opioids (PWUO) in syringe service programs (SSPs) in five Southeast U.S. cities with high HIV incidence and COVID-19 rates.
Methods: PWUO men and women (N=192) were part of a larger parent study, NIDA CTN-0082 (N=557), a one-time in-person survey on substance use, HIV risk behavior, and opioid use- and PrEP-related experiences and attitudes.
Results: Preliminary results showed widespread substance use in the past 12 months (heroin, n=159, 83%; fentanyl, n=144, 75%; other opioids, n=171, 89%; stimulants, n=179, 93%; alcohol, n=126, 66%; heavy drinking, n=96, 77%; marijuana, n=138, 78%; sedatives, n=109, 62%). Subgroups of PWUO reported more opioid use (n=64, 34%), non-opioid substance use (n=54, 28%), alcohol use (n=34, 18%), or distress (n=68, 36%) during the pandemic. Nearly one-quarter reported increased interest in medication for opioid use disorder (n=44, 23%) and opioid use counseling (n=41; 22%) during this time. However, the majority reported no change in use of opioids (n=111, 58%), non-opioids (n=122, 64%), alcohol (n=140, 73%), or distress (n=108, 57%).
Conclusions: Substantial, but not majority, subgroups attributed increased substance use or psychological distress to the pandemic. Already struggling with high rates of substance use and distress, over 50% of PWUO in SSPs reported the pandemic had not increased their substance use or distress. PWUO who frequent SSPs might be so inextricably bound to their substance use that even the widespread restrictions imposed by the pandemic did not disrupt or reduce access to substances. More work can be done to understand the relationship between the pandemic and SSP-using PWUOs' lifestyle choices.
Financial Support: This study is supported by grants from the NIDA National Drug Abuse Treatment Clinical Trials Network: UG1DA013035, New York, NY, PIs: John Rotrosen (NYU School of Medicine) and Edward Nunes (Columbia University Irving Medical Center and NY State Psychiatric Institute); UG1DA013714, Seattle, WA, PIs: Mary Hatch (University of Washington) and John Roll (Washington State University); UG1DA013720, Miami, FL, PIs: Daniel J. Feaster and Jose Szapocznik (University of Miami) and Lisa R. Metsch (Columbia University).

T43. Psychoactive Substance Use and Road Traffic Accidents Among Commercial Passenger Vehicle Drivers: A Scoping Review Protocol

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Other
Abstract Detail Human
Abstract Category Literature Review
Aim: To estimate the prevalence of psychoactive substance use by commercial passenger vehicle drivers and associated accidents or crashes. To find the gaps in the literature relating to psychoactive substance use by commercial passenger vehicle drivers.
Conclusions: This is a scoping review protocol only at the moment. The review process has just started. The results and conclusion will be presented as a poster during the conference.
Financial Support: NIDA INVEST Prevention Research Fellowship

T44. Religiosity, Religious Coping and Substance Use for Young Black Men After Trauma

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Young Black men (YBM) are at increased risk of trauma exposure compared to their white peers, yet YBM are less likely to utilize services for mental health treatment. Substance use is a common coping behavior among those who experience traumatic events, especially if the events are followed by symptoms of posttraumatic stress disorder (PTSD) or depression. However, religious coping and spirituality can also serve as a way to cope and promote healing. Although research has demonstrated the importance of

religiosity for many YBM, attitudes and importance of beliefs have varied, and some YBM expressed hesitation for religious coping. Thus, it is important to understand the relationships between religiosity and religious coping preferences of YBM with symptoms of posttraumatic stress, depression, and substance use.
Methods: This study was a secondary analysis of data from 55 YBM (18-30 years old) with previous trauma exposure, who were recruited from urban community settings (e.g., colleges, barbershops, churches) for participation in a mixed-methods study. Participants were on average 23 years old.
Results: Regression was conducted to examine the relationships between coping style and religiosity with symptoms of depression and substance use among YBM. Most participants (63%) thought of God at least daily, while 45% of participants reported rarely attending a worship service. Religiosity was not associated with depression or PTSD but did significantly predict lower lifetime substance use ($\beta = -.431$, $p = .011$), particularly for marijuana (OR = .918, $p = .034$). Religious coping was not significantly related to any outcome, but behavioral disengagement as a coping method was significantly associated with greater depression symptoms ($\beta = .897$, $p < .001$) and likelihood of PTSD (OR = 3.62, $p = .019$).
Conclusions: Results from this study may assist in the development of culturally relevant treatments that leverage spiritual coping processes among YBM.
Financial Support: National Institute on Drug Abuse (5R25DA035161-07, Multiple PIs: Ruglass and Hien), National Institute of Mental Health (R36MH115722-01, PI: Bauer)

T45. Social-Emotional Skills and Polysubstance Use Patterns Among Adolescents in Detention Facilities

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Nearly 60,000 children and adolescents are incarcerated in the United States, and many of them experience social-emotional problems and polysubstance use. Despite the known social and health risk factors, they are predisposed to stigma, harassment, and collateral consequences that can trigger or exacerbate substance misuse problems. Social-emotional learning (SEL) has been defined as the process of developing the self-awareness, self-control, and interpersonal skills that are critical for fostering resilience and positive life outcomes. In recent years, SEL has increased in popularity as a method to reduce harmful behaviors and unhealthy choices. However, there is a lack of research on the association between social-emotional skills and polysubstance use among incarcerated adolescents.
Methods: Multinomial logistic regression was employed to analyze a statewide sample of 79,960 JIA from the Florida Department of Juvenile Justice. This sample represents all youth who (a) received one or more arrests for delinquency, (b) completed the full intake assessment, and (c) reached the age of 18 by the year 2016. Polysubstance use was derived from self-disclosure. The level of social-emotional skills was operationalized using an index based on self-reported data.
Results: Over 90% of substance users in the sample were polysubstance users. Results indicate that social-emotional skills reduced the likelihood of polysubstance use, and their protective capacities varied by types of substances used.
Conclusions: Evidence suggests that social-emotional learning can potentially play a role in the prevention and treatment of substance misuse among adolescents. Juvenile justice agencies should investigate whether implementing social-emotional learning in their community reentry initiatives reduces relapse and recidivism.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

T46. Substance Use Treatment Utilization Among Individuals With Substance Use Disorders in the United States During the COVID-19 Pandemic: The Role of Polysubstance Use Criminal Justice Involvement

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: As overdose deaths skyrocketed during the COVID-19 pandemic, unprecedented social and economic issues increased barriers to treatment for substance use disorders (SUDs). Using a nationally-representative sample, we explore substance use treatment-seeking rates during the pandemic era among those with SUDs, emphasizing populations with high vulnerability (e.g., criminal justice involvement (CJI), polysubstance use, severe mental illness).
Methods: Data were derived from N=4,596 individuals with SUDs who completed the NSDUH (2020), representing 35 million non-institutionalized adults with SUDs in the US. DSM-5 criteria determined SUDs, while judicial supervision through parole or probation determined CJI. Substance use treatment was broadly defined (any inpatient, outpatient/doctor's office, self-help/other for alcohol/drugs). Logistic regression was used to assess the association of CJI, number of SUDs, and substance use treatment.
Results: Among adults with SUDs in 2020, 7 million (20%) had multiple SUDs, 1.75 million (5%) had CJI, 5.3 million (15%) had a severe mental illness, and only 7% sought any substance use treatment in the past year. CJI (aOR:12.78, 95%CI:7:41, 22.03), increase in the number of SUDs (aOR:1.94, 95%CI: 1.44, 2.61), and severe mental illness (aOR:3.17, 95%CI: 1.85, 5.43) were associated with increased odds of receiving treatment. Marriage (aOR:0.45, 95%CI: 0.26, 0.77) and having an income twice the poverty threshold (aOR:0.50, 95%CI: 0.27, 0.90) reduced the odds of receiving any substance use treatment. Compared to those 18-25, older individuals had increased odds (2-4 times) of receiving treatment. Race/ethnic differences in treatment utilization were evident among Asian-American individuals (aOR: 0.18, 95%CI:0.04, 0.87) compared to White individuals.
Conclusions: While populations with high vulnerability were more likely to receive substance use treatment, 93% of US adults with SUDs received no treatment in 2020. Interventions are crucially needed to increase access to treatment and the perception of treatment need among those with SUDs.
Financial Support: K01DA051715 (PI: Jones, A.A.)

T47. The Association Between Drug Use, Stressful Life Events, and Chaos With Participant Enrollment in Health Research: A Comparison of Two Person-Centered Approaches

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Enrollment of diverse populations in health research studies is lacking, leading to findings which compromise external validity and generalizability. We tested whether two person-centered recruitment approaches resulted in equally high rates of study enrollment among community members with and without drug use and recent stressful events.
Methods: Participants in the NIDA-funded Transformative Approach to Reduce Research Disparities Toward Drug Users (Navigation) Study (n=613) were recruited through the University of Florida's community engagement program HealthStreet and randomized into one of two intervention groups: Navigation as Usual (NAU), involving study matching through a Study Navigator, or Enhanced Navigation (N+), involving study matching plus individualized assistance through a Study Ambassador. Past 30-day drug use was assessed, and the presence and perception of stressful life events were evaluated using the Recent Life Chaos Questionnaire. Logistic regression models were used to examine the odds of study enrollment at the 90-day follow-up.
Results: At 90 days, 32.8% of participants were enrolled in a health research study, a rate which was significantly higher in the N+ group (40.5%) compared to the NAU group (25.1%). Enrollment in at least one research study was associated with receiving the N+ intervention as compared to the NAU intervention (aOR=2.05, 95% CI=1.43,2.94, p<.001). There were no significant associations or differences in enrollment rates based on recent stressful events, perceived life chaos, or past 30-day drug use.

Conclusions: The effectiveness of the enhanced person-centered approach to recruitment demonstrates the feasibility of enrolling those with recent drug use and more stressful life circumstances into research.
Financial Support: This research was supported by the National Institute on Drug Abuse under Award Numbers R01DA027951 (PI: Cottler) and T32DA035167 (PI: Cottler), as well as by the University of Florida Clinical and Translational Science Institute, which is supported in part by the NIH National Center for Advancing Translational Sciences under award number UL1TR001427.

T48. Trends in the Concurrent Use of Nicotine and Cannabis Among Adults, United States, 2013-2019

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: The most recent US prevalence estimates and time trends for concurrent nicotine and cannabis use in adults date back to 2012. Since then, cannabis legalization has proliferated, and the nicotine market has diversified such that a wider array of products may be co-used alongside cannabis. Updated estimates are needed to monitor emerging trends.
Methods: Data are from US adults who participated in Waves 1-5 (2013-2019) of the PATH Study (n=32,320). Prevalence of any past 30-day cannabis use, any nicotine use, and any co-use of nicotine and cannabis (including cannabis+cigarettes; cannabis+e-cigarettes) was calculated by wave. Crude time trends were examined using Generalized Estimation Equations on weighted data.
Results: Cannabis use increased from 6.8% in 2013-2014 to 12.6% in 2018-2019 ($p<0.001$). Any nicotine use declined from 29.0% in 2013-2014 to 27.5% in 2018-2019 ($p<0.001$); mainly driven by population-level reductions in cigarette smoking (21.9% in 2013-2014 vs. 19.3% in 2018-2019, $p<0.001$). Any co-use increased from 5.1% in 2013-2014 to 8.1% in 2018-2019 ($p<0.001$). Cannabis+cigarette co-use was consistently more prevalent than cannabis+e-cigarette co-use over time (cigarettes:4.3% in 2013-2014 vs. 5.8% in 2018-2019; e-cigarettes:1.6% in 2013-2014 vs. 3.7% in 2018-2019), yet the rate of increase was greater for cannabis+e-cigarette co-use (131%) than for cannabis+cigarette co-use (35%). Among nicotine users, cannabis use increased by an average of 12% at each wave (20.2% in 2013-2014 vs. 29.6% in 2018-2019, $p<0.001$). Among cannabis users, any nicotine use declined by an average of 13% at each wave (75.8% in 2013-2014 vs. 64.8% in 2018-2019, $p<0.001$).
Conclusions: While total nicotine use generally declined among US adults, co-use increased from 2013 to 2019. This appears to be driven by nicotine users adopting cannabis, rather than cannabis users adopting nicotine. Given the public health implications of co-use, future longitudinal analyses are needed to examine co-use adoption considering changing policies and markets.
Financial Support: This work was internally supported by the Department of Health Behavior at Roswell Park Comprehensive Cancer Center

T49. "The Talk to Me Like I Am a Human Being:" A Mixed Methods Analysis of Hepatitis Care Experience at Syringe Exchange Programs

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: This study examines people who inject drugs (PWID) stigma experiences with medical providers before and after engagement in Hepatitis C (HCV) care at a Syringe Service Program (SSP) in New York City.

Methods: As part of a randomized controlled trial to assess the effectiveness of HCV care collocated at SSPs, we recruited 167 eligible PWID for mixed method study. Eligibility criteria included positive HCV RNA, injection drug use in the 90-day period prior to enrollment, and no HCV treatment in the past 6 months. Analyses included the 71 participants randomized to receive HCV care at the SSP. In quantitative analyses, we compared validated healthcare stigma scores (MPS-PWUD scale) at study entry vs post-HCV engagement using Wilcoxon signed-rank test. Qualitative data analyses, based on semi-structured interviews with a purposively chosen subsample of 29 participants, focused on PWID experiences with medical providers.
Results: Participants (n=71) mean age was 42.6 (sd=11.03); 77% were males; 55% Hispanic; 30% Non-Hispanic White; 10% Non-Hispanic Black, and 58% recently homeless. Stigma scores significantly decreased from study entry to post-HCV engagement: overall (3.29 vs 2.36, p<0.01, Cohen's d effect size=0.966), enacted stigma (3.08 vs 2.11, p<0.01, Cohen's d effect size=0.982) and internalized stigma (3.73 vs 2.87, p=<0.01, Cohen's d effect size=0.685). Qualitative analyses indicate common experiences of stigma and dehumanization in health care settings prior to HCV care engagement at SSP. In contrast, participants reported their experiences with HCV care at SSP as "humanizing", "caring", "empathic", "non-judgmental" and "respectful".
Conclusions: HCV care collocated at SSP reduces enacted stigma from medical providers. Destigmatizing the healthcare experience is critical to promote HCV elimination efforts, which require increased treatment uptake among highly stigmatized groups, such as PWID.
Financial Support: This research was supported by NIH/NIDA Grant No. R01DA041298. Dr. Aponte-Melendez time was supported as a postdoctoral fellow in the Behavioral Sciences Training in Drug Abuse Research program sponsored by New York University with funding from the National Institute on Drug Abuse (5T32 DA007233).

T50. Barriers and Facilitators to COVID-19 Vaccination Among People Who Inject Drugs in San Diego County

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: To explore barriers and facilitators to COVID-19 vaccination among people who inject drugs (PWID), a population with suboptimal vaccine access and uptake.
Methods: From September-November 2021, we conducted qualitative interviews on experiences with preventive services with PWID ≥18 years old in San Diego County. Interviews were audio-recorded, transcribed, and coded for thematic analysis focused on identifying barriers and facilitators to COVID-19 vaccination.
Results: Among 28 participants, 15 reported receiving ≥1 COVID-19 vaccine dose at various locations, including community health centers, pharmacies, jails, and homeless shelters. Relating to vaccination barriers, we identified three core themes: risk assessment, institutional mistrust, and conflicting information. First, most unvaccinated participants did not view themselves at risk for COVID-19 and thus did not prioritize getting vaccinated. Several also expressed concerns about vaccine side effects, questioned how vaccination would help them personally, and explained that living on the streets had increased their immunity to SARS-CoV-2. Second, many participants expressed views of institutional mistrust leading to suspicions of government programs and medical treatments. Some participants also described rumors and conspiracy theories (e.g., involving pharmaceutical profits and government plans of population control) as reasons for vaccination campaigns. Third, many participants noted conflicting facts about COVID-19 vaccines disseminated via news and social media. Facilitators of vaccination that participants experienced or suggested as potentially helpful included increased vaccine education and accessibility, addressing concerns about governmental transparency, and considering the use of financial incentives.
Conclusions: Findings from qualitative interviews with a sample of PWID, only half of whom had been vaccinated for COVID-19, suggest a need for tailored intervention strategies to increase vaccine literacy and motivation (e.g., by emphasizing direct personal health benefits) while reducing structural barriers to access.

Financial Support: This work was supported by the San Diego Center for AIDS Research (National Institute of Allergy and Infectious Diseases, grant P30AI036214) with additional support from the National Institute on Drug Abuse (grants R01DA049644-S1, R01DA049644-02S2, K01DA043412, and 3K01DA043412-04S1), UC San Diego Altman Clinical and Translational Research Institute SUSTAIN program (NIH/NCATS 1KL2TR001444), and the California HIV/AIDS Research Program (CHRP, grant OS17-SD-001).

T51. Behavioral Health Benefits of Virtual Native American Talking Circles Group Sessions: Understanding the Impact of Peer Support Groups During COVID-19

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: Review use of Virtual Native Talking Circles (VNTC) related to the 2020-2021 COVID-19 Pandemic. Burn-out and turnover among behavioral health (BH) professionals was a serious threat to adequate BH services being provided in Native communities. Native BH professionals and community members have experienced serious consequences of the pandemic over the course of the past year; Native communities have had the highest rate of morbidity and mortality because of the pandemic, compared to any other ethnic group in the US. Considerations in conducting the VNTC in providing the VNTC will include key AI/AN cultural concept, application of the talking circle model in a virtual setting, protective factors related to VNTC model, impact statements from participants of the VNTC and the qualitative data supporting the essential role Native ceremony can play in the health and wellbeing of the Indigenous people of this nation
Methods: VNTC met bi-weekly via zoom beginning April 9, 2020 and was facilitated by Fred Little Bald Eagle of the Rosebud Nation in SD. Number of events: 22, total number of participants: 1246.
Results: Results from the GPRA surveys for each event beginning April 9, 2020 (N=321) and a 17-question Qualtrics satisfaction survey with both Likert and short answer questions administered beginning February 9, 2021 (N=51), will be shared with participants. 100% of the 321 completed GPRA surveys showed that they would recommend this event to a colleague or friend. The feedback and data reviewed and collected thus far suggest the important supportive and connectiveness that is afforded by those engaged in this type of virtual group.
Conclusions: The implications of our program will show the potential health/ wellness benefits created through regular attendance to Virtual Native Talking Circles over the course of an extended global pandemic calendar year.

T52. Best Practices for Substance Misuse Research Education Programs to Promote Diversity, Equity, and Inclusion

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Policy
Abstract Detail Human
Abstract Category Theoretical/Commentary
Aim: National and global substance misuse problems require a diverse workforce of researchers with a kaleidoscope of backgrounds, perspectives, and talents. However, due to multidimensional historical and social factors, certain groups remain underrepresented in the field. Subsequently, in the past year, there have been unprecedented investments in research education programs to enhance diversity. However, there is a lack of information and resources to guide the development of these programs. The current study synthesizes limitations, solutions, and best practices for substance misuse research education programs that intend to promote diversity, equity, and inclusion.
Methods (Optional): The current study leverages observational, anecdotal, and qualitative data from six research education programs that have identified diversity, equity, and inclusion as a primary function of the

program. Basic thematic coding was used to identify major themes. Deviant case analysis was employed to improve internal validity.
Results (Optional): The results indicate that persons who identify as Black, Latinx, Indigenous, and persons of color face similar challenges while matriculating traditional education systems that can have long-term adverse consequences. These challenges include stigma, financial burdens, deficits in early education, inadequate mentoring, few enrichment opportunities, cultural homogeneity, uncomfortable climates, micro-aggressions, discriminatory attitudes, social adversities, and other obstacles. These challenges can have a domino effect throughout graduate school and throughout one's career to adversely affect employment, tenure qualifications, and other aspects of academic life. Trainees tend to value programs that understand, discuss, and seek to address these issues in their capacities. In addition, research experiences that encompass culturally relevant pedagogy, mentoring relationships with diverse role models, and intensive student-faculty and peer interactions can help offset the systematic barriers.
Conclusions: In conclusion, to Promote Diversity, Equity, and Inclusion in the field of substance misuse, research education programs should improve their recruitment efforts and ensure that their programs provide early and ample exposure to rigorous and culturally relevant training.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

T53. Concurrent Sleep-Motivated Non-Medical Use of Prescriptions and Substance Use: A Latent Class Analysis

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: With 1 in 3 adults sleeping less than recommended, many endorse non-medical use (NMU) of prescription tranquilizers/sedatives to improve sleep. Concurrent substance use (CSU) among these individuals is common, therefore we identified patterns of past 12-month (P12M) CSU among adults reporting P12M sleep-motivated NMU of tranquilizers/sedatives.
Methods: Data from the 2015-2019 National Surveys on Drug Use and Health observed differences among individuals aged 12+ with and without P12M sleep-motivated NMU of tranquilizers/sedatives (n=282,768). Then, participants endorsing P12M sleep-motivated NMU of prescription sedatives/tranquilizers were included in latent class analyses to identify distinct classes of P12M CSU (n = 3,097).
Results: Participants with sleep-motivated NMU had significantly higher rates of P12M major depressive episodes (NMU: 25.8% vs. no NMU: 6.9%) and P12M substance use and prescription NMU. Four CSU classes were identified: 1) "alcohol CSU" class (41.2%), 2) "tobacco/alcohol/marijuana CSU" (37.1%), 3) "diverse CSU" (16.0%), and 4) "alcohol/marijuana/NMU of prescription pain relievers" (5.7%). The "diverse CSU" class was the only class to have a significant difference between sexes (males: 61.7%). Furthermore, younger participants were more likely to fall into the "diverse CSU" class, while participants aged 50+ had a greater likelihood of falling into the "alcohol CSU" class.
Conclusions: While some characteristics associated with sleep-motivated NMU are common, variations in P12M CSU are apparent. Future work should investigate simultaneous use with NMU of tranquilizers/sedatives, particularly when it results in severe adverse outcomes, such as increased mortality risk associated with co-use of prescription tranquilizers/sedatives and alcohol.
Financial Support: This research was supported by the National Institute on Drug Abuse T32 training grant at the UF Substance Abuse Training Center in Public Health from the National Institutes of Health (T32DA035167, Cottler, PI) and Mentored Research Scientist Development Award (K01DA046715, Lopez-Quintero, PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

T54. Internalized Stigma Among Legal-System Involved Women in Substance Use Disorder Treatment

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The World Health Organization ranked drug addiction as one of the most stigmatized health conditions globally. Stigma is negatively associated with treatment seeking and successful recovery among individuals receiving treatment for a substance use disorder (SUD). Legal-system involved women are at an increased risk for experiencing stigma, and legal-system related stigma is positively correlated with recidivism, substance dependence, mental health symptoms, and poor community adjustment among women. Participants included in the current secondary analysis study participated in a randomized clinical trial of mindfulness-based relapse prevention (MBRP) versus relapse prevention (RP) as treatments for SUD.
Methods: Internalized shame was measured using the Internalized Shame Scale (ISS) during baseline, follow-up, and post-treatment visits. Two latent growth curve models of the ISS total scores where then estimated over time to examine (1) the intercept and slope of ISS scores regressed on treatment condition, and (2) the change in ISS scores within each treatment condition separately.
Results: Results from the growth model regressed on treatment indicated significant reductions in internalized shame scores during treatment (slope = -11.26 (SE=5.07), p = .03). Treatment condition was not significantly related to intercept (β = -0.03; B (SE) = -1.75 (6.81), p=0.80) or nonlinear slope (β = -0.30; B (SE) = -5.46 (6.04), p=0.37). Results from the growth model by treatment groups indicated significant reductions in ISS scores over time in both treatment conditions, with larger reductions in MBRP (slope = -16.33 (SE=4.99), p = .001) than RP (slope = -10.85 (SE=4.73), p = .02).
Conclusions: Although we observed significant reductions in internalized shame from pre- to post-treatment, differences across treatment conditions were not statistically significant. Additional research is needed to determine how distinct treatment components relate to reductions in internalized shame among individuals receiving treatment for SUD.
Financial Support: 4UH3DA051241-03, 4UH3DA051241-03-S1

T55. Leaving the Military in the Context of Mental Health Problems: Does It Increase Risk for Drug Use?

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Research has consistently demonstrated relationships between mental health problems and drug use among military populations, but less is known about the additional effects of leaving the military – a major time of transition. Our aim was to examine the effects of leaving the military on illicit drug use and non-medical use of prescription drugs (NMUPD). We hypothesized that those who left the military would have a greater risk of drug use, compared to those still serving, and that those leaving the military with greater mental health symptomatology would be at greatest risk.
Methods: Data were drawn from the fifth wave of Operation: SAFETY, an ongoing longitudinal survey study of US Army Reserve and National Guard soldiers (N=394 current/former soldiers). Logistic regression models assessed the relationship between military status (current/former) on past year and current illicit drug use and NMUPD, controlling for sex and deployment history (ever/never). An interaction term was added to each model to examine whether leaving the military in the context of symptoms of anxiety, anger, depression, and PTSD was related to drug use, separately.
Results: Former soldiers had greater odds of past year (OR: 4.34; 95% CI: 2.17, 8.69; p<.001) and current illicit drug use (OR: 4.25; 95% CI: 2.00, 9.24; p<.001), compared to current soldiers. Military status was not

related to past year or current NMUPD. All interactions between military status and each of the mental health variables were non-significant, indicating that mental health symptoms do not affect the relationship between military status and illicit drug use.
Conclusions: Leaving the military, in and of itself, may increase the risk of illicit drug use, regardless of mental health symptomatology. Further research is needed to examine these relationships over time and identify other mechanisms, beyond mental health, which may contribute to this increased risk for former soldiers.
Financial Support: This research was supported by the National Institute on Drug Abuse award number R01DA034072 to Gregory G. Homish and by the National Center for Advancing Translational Sciences of the National Institutes of Health under award number UL1TR001412 to the University at Buffalo.

T56. Major Depressive Episodes Among U.S. Adults Who Use Kratom (Mitragyna Speciosa): Concurrent Substance Use Patterns and Sociodemographic Differences

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Kratom (Mitragyna speciosa), a relatively novel and legal psychoactive substance, has reportedly been used to self-treat mood disorder symptomology, such as depressive feelings. However, the scientific community has yet to assess potential effectiveness and efficacy of kratom to alleviate depressive symptoms. Additionally, it is unknown whether demographic and socioeconomic differences exist between kratom users who experience vs. do not experience depression. This retrospective study investigated association between past-year kratom use and past-year major depressive episode (MDE) among adults in the United States (U.S.). Further, differences in past-year substance use, as well as social, demographic, and economic characteristics among past-year kratom users with vs. without past-year MDE, were assessed. We hypothesized that significant differences between these subpopulations would be revealed.
Methods: Chi-square tests and multivariate regression models were conducted using a nationally representative sample of U.S. adults (weighted n=247,278,766), gathered via the 2019 National Survey on Drug Use and Health (NSDUH). Statistical analyses were conducted in R.
Results: When examined independently, the proportion of U.S. adults with past-year kratom use who reported 1) past-year use of alcohol (94% vs. 82%; p=0.018) and 2) past-year prescription tranquilizer or sedative use (56% vs. 39%; p=0.037) was greater among those endorsing past-year MDE, compared to kratom users without past-year MDE. Past-year marijuana use approached significance (75% vs. 62%; p=0.051). No statistically significant differences were observed for selected socioeconomic and demographic factors (i.e., age cohort, employment status, family income, health insurance status, perceived health status, racial identity, and sex) nor past-year use of the following substances: cocaine, hallucinogens, prescription pain relievers, prescription stimulants, or tobacco.
Conclusions: These findings suggest that medical providers, psychiatrists, and addiction specialists treating patients who disclose past-year use of kratom and past-year MDE should inquire on the patient's use of other substances to tailor treatment plans towards the patient's unique healthcare needs.
Financial Support: The first and second authors are supported by the UF Substance Abuse Training Center in Public Health from the National Institute of Drug Abuse (NIDA) of the National Institutes of Health under award number T32DA035167 (PI: Dr. Linda B. Cottler). The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the National Institutes of Health.

T57. Perceived Link Between COVID-19 and Substance Use and Mental Health: Findings From Men Who Have Sex With Men Who Use Substances Visiting Sexually Transmitted Infection Clinics in Southeast U.S. Cities

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Other
Abstract Detail Human
Abstract Category Original Research
Aim: Men who have sex with men and use substances (SU-MSM) are at increased risk for HIV. COVID-19 has impacted healthcare delivery including sexually transmitted infection (STI) services accessed by SU-MSM, yet little is known about the impact on key health indicators from their perspective. This study examined the perceived link between COVID-19 and substance use, pre-exposure prophylaxis (PrEP) interest, sexual behavior, and mental health among SU-MSM visiting STI clinics in five Southeast U.S. cities with high HIV and COVID-19 rates.
Methods: While at the STI clinic, SU-MSM (N=146) completed an online survey that focused on substance use, HIV risk behavior, and experiences with and attitudes toward opioid use- and PrEP-related services.
Results: Preliminary results show that, in the prior 12 months, a majority of participants reported alcohol use (n=142, 97%) and heavy drinking (5+ drinks if born male and 4+drinks if born female, in one sitting) (n=132, 93%) at least once; SU-MSM also used marijuana (n=82, 57%), poppers (n=56, 39%), stimulants (n=43, 29%), and opioids (n=8, 5%). In response to the pandemic, roughly one-third reported increased alcohol use (n=52, 36%). Most saw no change in opioid use (n=131, 90%) or drug use other than opioids (n=117, 80%). Almost half (n=68, 47%) reported no change in sexual activity, but 20% reported increased (n=28) and 34% (n=50) reported decreased sexual activity; 17% (n=25) reported increased interest in PrEP. Forty percent (n=57) reported feeling greater psychological distress.
Conclusions: SU-MSM in STI clinics maintained or increased their already high rates of substance use during the pandemic. Sexual activity continued and a substantial proportion struggled more with their mental health. Examining the challenges and resilience resulting from the pandemic suggests that HIV prevention services need to adapt and innovate and provides a foundation for innovative delivery of HIV prevention services and implementation research.
Financial Support: This study is supported by grants from the NIDA National Drug Abuse Treatment Clinical Trials Network: UG1DA013035, New York, NY, PIs: John Rotrosen (NYU School of Medicine) and Edward Nunes (Columbia University Irving Medical Center and NY State Psychiatric Institute); UG1DA013714, Seattle, WA, PIs: Mary Hatch (University of Washington) and John Roll (Washington State University); UG1DA013720, Miami, FL, PIs: Daniel J. Feaster and Jose Szapocznik (University of Miami) and Lisa R. Metsch (Columbia University).

T58. Racial Differences in the Association Between Family Functioning and Substance Use Disorder Treatment Completion Among Justice-Involved Adolescents

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Justice-involved adolescents have a significantly higher prevalence of substance use disorders and can face harsher consequences from drug use than adolescents in the general population. However, only a fraction of justice-involved adolescents complete a treatment program, and racial/ethnic minorities tend to have poorer treatment outcomes. Identifying the major factors that improve treatment outcomes for diverse racial groups is critical. Family-level resources are powerful protective factors, especially for certain racial/ethnic groups, and may be linked to treatment adherence. The current study is the first to investigate racial differences in the association between family functioning and substance use disorder treatment completion among justice-involved adolescents.
Methods: Logistic regression was employed to analyze a statewide sample of 35,865 adolescents from the Florida Department of Juvenile Justice. This sample represents all adolescents who received an arrest for delinquency, completed the full intake assessment, reached the age of 18 by the year 2016, and initiated a treatment program. Substance use disorder and family functioning was were both derived from self-reported

data. Family functioning refers to the quality of interactions and relationships within a family, including cohesion, adaptability, organization, communication, and levels of conflict.
Results: Higher levels of family functioning were associated with higher odds of treatment completion in the total sample. Once stratified by race, the relationship was greater for Black adolescents relative to White adolescents and not significant among Latinx adolescents.
Conclusions: The results of this study suggest that family-based and home visitation interventions may be especially important to improve treatment adherence among justice-involved adolescents, especially those who are Black. The justice community should invest in leveraging family resources in their intervention programs.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

T59. Racial Discrimination, Historical Trauma, Racial Microaggressions and Polysubstance Use in Black Young Adults

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Historical trauma is the collective psychological injury inflicted on a multigenerational group of people with shared identities and is associated with increased substance use. Although Black youth may be negatively impacted by historical displacement and loss of ancestry very little empirical research has connected these experiences with present-day violence rooted in racism, marginalization, and oppression. This study examines the associations between historical loss, racial microaggressions, major racial discrimination events, and polysubstance use among Black young adults.
Methods: Predominantly female (63.2%), self-identified Black individuals (N = 57), aged 18-35 (M = 26.1, SD = 4.56) were recruited from colleges across the Northeastern US to complete an online survey (data collection ongoing). Pearson's r correlations and multivariate linear regressions were conducted to examine the associations between experiences of historical loss, racial microaggressions, major racial discrimination events, and past 12-month polysubstance use (count of 2 or more unique substances used).
Results: Half the sample engaged in polysubstance use (50.9%). Significant positive correlations were observed between past year polysubstance use behaviors and historical loss symptoms ($r = 0.50$, $p < 0.001$), racial microaggressions ($r = 0.55$, $p < 0.001$), and major racial discrimination events ($r = 0.74$, $p < 0.001$). After accounting for historical loss symptoms and racial microaggressions, major racial discrimination events were still significantly associated with past year polyuse ($R2 = 0.57$, $B = 0.51$, $t = 5.52$, $p < 0.001$).
Conclusions: These results expand the historical trauma literature and suggest that Black youth may not only use substances to cope with current race-based stressors, but also to cope with historical trauma. Major racial discrimination events were a persistent risk factor for polysubstance use when accounting for historical trauma and racial microaggressions. This finding suggests the potential broader impact of racism, within the context of historical trauma, on substance use outcomes among Black young adults.
Financial Support: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Drug Abuse. This research was supported by a grant from the National Institute on Drug Abuse (5R25DA035161-07, Multiple PIs: Ruglass and Hien) and by The New School for Social Research Travel Fund Award.

T60. Resilience During the COVID-19 Pandemic Among Persons Who Use Non-Injected Heroin and Cocaine: Resistance to Injecting, Stable Mental Health, and Reduced Heroin and Cocaine Use

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Originally, to field test "Avoid the Needle," a psychosocial intervention to reduce the likelihood that non-injecting drug users (NIDUs) would transition to injecting drug use. When the study was interrupted by the COVID-19 pandemic "lockdown," an aim of examining drug use during the pandemic was added. There was a general concern that the pandemic would lead to increased drug use and increased transitions to injecting drug use.
Methods: Beginning in late 2019, 153 NIDUs were recruited through respondent driven sampling and participated in a baseline interview and in "Avoid the Needle," a psychosocial intervention based on motivational interviewing, cognitive behavior theory and skill practice, to reduce the likelihood of transitions to injecting. In March 2020, in-person interviewing was halted due to the pandemic, and the study changed to telephone for follow-up interviews beginning in June 2020.
Results: We were able to re-establish contact with conduct follow-interviews with 83 (54%) subjects. All subjects reported substance use disorders (SUDs) at baseline, with 94% for heroin or cocaine. Mean age 56, (SD 9). 59% reported never having injected drugs; 41% reported having previously injected but not within the 6 months prior to baseline. No subjects transitioned to injecting drug use at the mean 9-month follow-up interviews. Mental health (Kessler 6) was quite stable, with 73 reporting no change in status, 6 reported deterioration, and 4 reported improvements. There were significant changes in frequencies of heroin/cocaine use: 8 increased frequency, 23 remained at same frequency, 19 reduced frequency but continued using, and 23 ceased using ($p=0.001$ for reduction in frequency).
Conclusions: These long-term, experienced non-injecting heroin and cocaine users are likely to have developed considerable resilience to maintain health during changes in drug environments. Future interventions should capitalize on such resilience to reduce harms associated with heroin and cocaine use.
Financial Support: This work was supported through grant 5-DP1-DA039542 from the US National Institute on Drug Abuse. The funding agency had no role in the design, conduct, data analysis or report preparation for the study.

T61. Substance Use Trajectories Among Urban College Students: Associations With Symptoms of Stress, Anxiety, and Depression Before and During COVID-19

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: This study sought to explore substance use trajectories and associations with mental health among an ethnically/racially diverse college student sample before and during the coronavirus disease 2019 (COVID-19) pandemic.
Methods: We combined repeated cross-sections and panel data from a total of 3,247 college students (69% women, 80% non-White) assessed with an online survey in 2018, 2019, and in three waves in 2020. We estimated trends in substance use (assessed with Quantity-Frequency measures of cigarette/e-cigarette, alcohol, cannabis, and other substance use), and their relation to mental health (Depression, Anxiety and Stress Scale-21) over the survey waves using generalized estimating equations (GEE).
Results: Our results revealed notable associations between 30-day substance use patterns, time of assessment, and psychological well-being. While cigarette or e-cigarette use did not vary significantly over time, the odds of having used alcohol were lower in all three 2020 waves. In contrast, compared to 2018, odds of having had at least one binge drinking episode (relative to no episodes) were significantly higher in the last two waves of 2020 (2020_2: OR=2.46, $p<.001$; 2020_3: OR=2.99, $p<.001$). Likewise, the odds of having used cannabis in the past 30 days were higher in the last wave of 2020 (OR=1.40, $p<.05$). On average, students' symptoms of stress, anxiety and depression were within the normal range at all time

points. However, increases in stress levels were associated with the likelihood of cannabis and alcohol use, binge drinking, and use of other substances.
Conclusions: Our findings suggest a complex interplay between access to substances, context of substance use, and mental health. Several initiatives (e.g., a peer-support system) have been launched locally in response to the results of this ongoing study. Such initiatives may serve as examples for expanding similar efforts to other commuter colleges to prevent further increases in mental health problems and risky substance use.
Financial Support: This work was supported by a grant from the New York State Office of Addiction Services and Supports (PI: Robert Melara). Laura Brandt is funded by an INVEST/CTN Drug Abuse Research Fellowship from the National Institute on Drug Abuse.

T62. The Impact of COVID-19 on Mental Health and Substance Use Outcomes Among Queer Women of Color: A Scoping Review

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Abstract Detail Human
Abstract Category Literature Review
Aim: Sexual and gender minorities (SGM) experience striking health disparities than their heterosexual counterparts, including worse mental and physical health outcomes. The COVID-19 pandemic has been associated with increases in depression, anxiety, and substance use. We conducted a scoping review to examine the experiences of SGM women of color during the COVID-19 pandemic and specifically the impact on mental health and substance use outcomes.
Methods (Optional): Following PRISMA guidance, we searched published literature between January 2020 to December 2021 using PubMed, PsycINFO, PsycArticles (ProQuest), and Google Scholar. Publications that met the following criteria were included: quantitative or qualitative studies, published in English, focus on COVID-19 pandemic stressors and mental health and substance use outcomes, specific data on SGM women of color. Studies focusing primarily on sexual gender minority men were excluded.
Results (Optional): A preliminary search identified 26 studies (n = 23 quantitative and n = 3 qualitative studies) that met criteria. Studies demonstrated SGM women of color reported worse mental health and problem drinking compared to cisgender heterosexual women. SGM were also more likely to be impacted by the effects of COVID-19 with increases in depression and anxiety. College-age SGM students exhibited high levels of psychological distress associated with campus closure and initiation of alcohol use to cope specifically with boredom and isolation.
Conclusions: The ongoing COVID-19 pandemic appears to exacerbate SGM women of color's mental health and substance use outcomes. Research is needed to explore the social determinants that lead to SGM experiencing poorer mental health and greater substance use and the potential for tailored interventions to address these outcomes.
Financial Support: National Institute on Drug Abuse (5R25DA035161-07, Multiple PIs: Ruglass and Hien

T63. Types of Traumatic Experiences in Drug Overdose-Related Deaths: An Exploratory Latent Class Analysis

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Drug overdose related-deaths in the US are increasing, with over 93,000 deaths occurring in 2020, an increase of 30% from the previous year and the highest number recorded in a single year. It is widely known

that experiences of trauma and substance use highly overlap, but little is known about the role of trauma in the context of drug overdose-related deaths. This latent class analysis (LCA) sought to classify drug overdose-related deaths based on types of traumatic experiences and substance use types.
Methods: Psychological autopsy data were obtained from the University of Texas Health Science Center at Houston (UTHealth) Brain Collection. A total of 26 drug-related deaths collected between January 2016 to January 2021 were included in this study. LCA was used to identify latent factors via experience of four trauma categories (illness/accidents, sexual/interpersonal violence, death/trauma to another, other situations where life was in danger). Generalized linear modeling (GLM) was used to explore differences on each demographic, social, substance use, and psychiatric variable between the latent classes in separate models.
Results: LCA identified 2 classes: C1 (n=14, 54%) was characterized by higher incidence of overall trauma, with sexual/interpersonal violence and experiencing death/trauma to another person as most frequent; C2 (n=12, 46%) had lower levels of overall trauma exposure, with less exposure to sexual/interpersonal violence than C1. GLMs indicated that C1 membership was associated with higher incidence of polysubstance use, being married, and having suicidal ideation compared to C2 membership (p's<0.05).
Conclusions: Among individuals who died by drug overdose, the exploratory LCA identified two distinct subgroups that differed in type of trauma experienced and substances used. If replicated, polysubstance use, marital status, and suicidal ideation differences found between the latent classes could potentially inform future risk reduction and overdose prevention efforts.
Financial Support: This study was supported by R01DA044859 to Consuelo Walss-Bass, PhD.

T64. Differences in Substance Class Use Among Driving Under the Influence of Drugs Events Using Real-Time Motor Vehicle Crash Data in the United States From 2019 to 2022

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Drug Category Other, Opioids, Methamphetamine, Non-opioids (LSD, Cannabis, Cocaine, Psychodysleptics)
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Driving Under the Influence of Drugs (DUID) has increased; however, data on substances involved in DUID is scarce; most are 6-months behind. This study aims to compare the means of DUID Motor Vehicle Crashes (MVC) by substance type from July 2019 to December 2021 using real-time Motor Vehicle Crash Data in the United States.
Methods: County-level EMS dispatch data from 19 states, updated within 24-hours, was used for a retrospective analysis (biospatial, Inc.). Data were summarized by 6-month periods from July 2019 to December 2021. The mean rate of non-fatal MVCs for each substance was calculated and adjusted for variation in reporting and population size. We used Poisson regression for the analysis. The sample to date is 10,186 individuals, including both sexes.
Results: The sample to date is 10,186 individuals (62.4% male, 59.3% non-Hispanic white and 32.5% 30-39 years old). Overall, DUID events were highest during July to December 2021. For all periods, methamphetamine were the most commonly used substance used in DUID MVC. Opioids were the second most common. Non-opioid use in the DUID MVC was lowest. When comparing between substances, the mean rate of DUID MVC for opioids was 1.73 times and for methamphetamine 1.60 times the rate for non-opioids.
Conclusions: When comparing the presence of methamphetamine, opioid, and non-opioid drug-attributed non-fatal MVCs, methamphetamine was the most prevalent. To the best of our knowledge, this study is the first in comparing DUID MVC by substance groups using real-time data.
Financial Support: Nae Yeon Won was supported by the UF Substance Abuse Training Center in Public Health from the National Institute of Drug Abuse (NIDA) of the National Institutes of Health under award number T32DA035167 (PI, Linda Cottler). The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the National Institutes of Health.

T65. The Association Between Potentially-Traumatic Events and Cocaine, Cannabis, and Alcohol Use Differs by Race

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Drug Category Other, cocaine, cannabis, and alcohol
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: The association between trauma and substance use is well-established, but less is known regarding racial/ethnic (r/e) group differences. Although exposure to potentially-traumatic events (PTE) for Black/African American (Blk/AA) and Latino/a/x/Hispanic people (Lx/Hisp) are comparable or lower than their White counterparts, type of trauma experiences differ such as more interpersonal trauma and violence reported by Blk/AA people, who also experience higher rates of PTSD.
Methods: In this retrospective study, we examined race-group differences for the association between PTE and substance involvement for alcohol, cannabis, and cocaine use (AUDIT; NIDA-modified ASSIST). Participants were 168 Blk/AA, Lx/Hisp, and White individuals from an outpatient substance use disorder program in Houston, Texas. All genders were included in this study. Bayesian generalized linear modeling with horseshoe prior was used to predict substance involvement using 17 PTE (LEC-5), then the PTE ranked and examined by r/e group.
Results: Of the PTE, only two traumatic events were associated with substance involvement across all three r/e groups: natural disaster and explosion. Notably, the three PTE involving interpersonal violence in our study (weapon assault, physical assault, and sexual assault; posterior probability ≥ 70%) were more strongly associated with substance involvement for Blk/AA and Latino/a/x individuals than White individuals.
Conclusions: The relational nature of interpersonally-violent traumas may make them particularly salient for r/e minority groups where interpersonal relationships are prioritized. These types of traumas may also be viewed as an extension of discrimination and exclusion, two longstanding, intractable issues for people of color in the US, making them even more damaging. Furthermore, lack of resources and knowledge may limit options for coping, resulting in substance use problems. Next steps are to replicate these results with larger samples, then further elucidate the mechanisms of interpersonal trauma that may lead to substance use for Blk/AA and Lx/Hisp people.
Financial Support: This study was supported by TI080734-01 to Angela Heads, PhD

T66. The Chemokine Antagonists Maraviroc and AMD3100 Reduce Opioid and Stimulant Choice in Rats

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Drug Category Other, Opioids and stimulants
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Decades-long efforts have led to the development of medications preventing substance misuse; however, few effective treatments have been identified. The neuroimmune system enhances dopamine signaling using chemoattractant cytokines (“chemokines”). These studies aimed to characterize the effectiveness of various chemokine receptor antagonists to reduce the reinforcing effects from stimulant (cocaine) and opioid (fentanyl) drugs using a food versus drug choice procedure in rats.
Methods: Adult male Sprague Dawley rats (n=16) were trained to respond under a fixed ratio (FR) 5 schedule of reinforcement on one lever to receive a drug infusion (0.032 mg/kg/inf cocaine; 0.0032 mg/kg/inf fentanyl) or a grain pellet (food) on the opposite lever. Rats then responded under a five-component choice procedure. Food was available throughout each 20 min component, and in components 2-5, ascending doses of drug (cocaine: 0.032-1 mg/kg/inf; fentanyl: 0.00032-0.01 mg/kg/inf) became available. After rats achieved stable responding, they were pretreated with: the μ-opioid antagonist naloxone (1, 3.2 mg/kg, IP); a dopamine D2-like antagonist haloperidol (0.01-0.1 mg/kg, IP); a CC Chemokine Receptor 5 antagonist, Maraviroc (3.2-17.8 mg/kg, IP); and a CXC Chemokine Receptor 4 antagonist, AMD3100 (3.2-17.8 mg/kg, IP) 15 min before choice sessions.
Results: Pretreatment with naloxone and haloperidol were positive controls to fentanyl and cocaine respectively, shifting responding away from drug and toward food. Maraviroc (10 mg/kg) decreased drug choice, and responding shifted toward food when lower doses of cocaine and fentanyl were available. The

highest dose of Maraviroc (17.8 mg/kg) disrupted initial responding for food in most animals. Pretreatment with AMD3100 (10-17.8 mg/kg) also diminished drug choice without altering selection for the non-drug reinforcer.
Conclusions: The chemokine antagonists Maraviroc and AMD3100 can reduce the reinforcing effects of opioid and stimulant drugs on rats during a choice procedure. The reduction of proinflammatory chemokine signaling may be a viable strategy to treat substance use disorders.
Financial Support: NIH R01 DA039146 (GTC); T32DA031115 (BM); VA I01 BX004550 (GTC)

T67. REL-1017 (Esmethadone; d-Methadone), a Rapid-Acting Antidepressant Has No Meaningful Opioid Abuse Liability in Nonclinical and Clinical Abuse Potential Studies

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Drug Category Opiates/Opioids
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: REL-1017 (esmethadone) is the opioid-inactive isomer of methadone and a novel uncompetitive NMDAR antagonist with efficacy in all tested models of depressive-like behaviour. In a Phase 2 clinical trial REL-1017 showed rapid, robust, and sustained efficacy as adjunctive treatment for Major Depressive Disorder (MDD) without opioid-like side effects. Phase 3 trials are in progress. Due to the high prevalence of substance use disorder among patients with MDD, we evaluated REL-1017 in nonclinical (rat) and human abuse potential (HAP) studies.
Methods: 1) Two nonclinical studies: intravenous self-administration (6 rats/group; saline, vehicle, oxycodone, or four doses of REL-1017: 0.032, 0.056, 0.1 and 0.18 mg/kg), and a withdrawal study [16 rats/group; saline, REL-1017 (62.5 or 100 mg/kg), ketamine (200 mg/kg) or morphine (300 mg/kg)].
2) HAP study: single-dose, randomized, double-blind, double-dummy, active- and placebo-controlled, 5-way crossover study of REL-1017 in recreational opioid users. These studies were performed according to the FDA's 2017 Abuse Potential Guidance.
Results: 1) Nonclinical studies: In the self-administration study oxycodone was a strong reinforcer whereas REL-1017 at all doses, showed saline-like patterns. In the withdrawal study, discontinuation of daily morphine and daily ketamine produced withdrawal signs. REL-1017 did not engender withdrawal signs after discontinuation.
2) HAP: 44 randomized subjects met analysis criteria; all tested REL-1017 doses, including the 150 mg dose (maximum tolerated dose and 6X the daily therapeutic dose), exhibited at least a 20-point difference in Emax Drug Liking, assessed with a bipolar (0 to 49 = dislike; 50 = neutral; 51-100 = like) visual analog scale (VAS), compared to 40 mg oxycodone, with a highly significant difference ($p<0.001$).
Conclusions: Controlled Substances Act scheduling of new chemical entities is based on the analysis of multiple factors, including nonclinical and HAP studies. These nonclinical and clinical studies did not show meaningful opioid-like abuse potential for REL-1017, consistent with prior publications.
Financial Support: Relmada Therapeutics, Inc.

T68. Racial and Ethnic Differences in Long-Term Outcomes After Randomization to Methadone or Buprenorphine/Naloxone Treatment for Opioid Use Disorder

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Drug Category Opiates/Opioids

Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Racial and ethnic differences in access and outcomes of medication treatment for opioid use disorder (OUD) have been of concern in the addiction field. Furthermore, little is known about their differences in long-term outcomes. This study examined racial and ethnic differences in long-term outcomes among individuals with OUD in a multi-site randomized clinical trial.
Methods: The study included 653 participants with OUD (10.0% were black, 12.3% Hispanic, and 77.6% white) who completed baseline and follow-up assessments during the follow-up period (mean of 6.7 years, SD=1.3). To test racial/ethnic differences, we used the Chi-square test for categorical variables and ANOVA for continuous variables. Bonferroni corrected and Tukey-Kramer methods were applied for pairwise comparisons.
Results: At baseline, black participants were older (Mean: 48.9 for black vs. 41.3 for Hispanic, 35.5 for white; $p<0.001$) and more reported using cocaine (black: 53.0% vs. Hispanic: 28.8%, white: 32.0%; $p<0.01$), while Hispanic participants had a higher proportion of injection drug use (Hispanic: 76.3% vs. black: 51.5%; $p<0.05$). More Hispanic participants had Bipolar 1 disorder (Hispanic: 23.3% vs. white: 11.5%; $p<0.01$) and mood disorder with psychotic features (Hispanic: 16.4% vs. white: 5.6%; $p<0.01$). Participants reported 54.1% of the time being on medication for OUD over the follow-up period; no racial/ethnic difference was found. At the end of the follow-up period, Hispanic participants had significantly greater severity in the employment domain (measured by the ASI) and the least number of years of opioid abstinence (Mean: 1.5 for Hispanic vs. 2.3 years for white; $p<0.05$).
Conclusions: While there were no group differences in our study sample regarding treatment participation, all groups may benefit from longer retention in medication treatment for OUD if needed. In addition, efforts to address factors (e.g., polydrug use, mental health, employment) adversely impact racial minorities may help improve their long-term outcomes.
Financial Support: This study was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number UG1DA049435, UG1DA013714, and UG1DA050067.

T69. Self-Reported Substance Use With Clinician Interviewers Versus Computerized Surveys

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Potentially underreported substance use is often listed as a limitation of survey studies; however, little is known about the agreement between different survey methods for capturing self-reported substance use. The current study therefore used repeated measures to compare self-reported use of alcohol, cannabis, cocaine, heroin, and prescription opioids using (1) clinician interviewers, and (2) self-administered computerized surveys.
Methods: Participants were adults age ≥18 years with substance use (cannabis, cocaine, opioid use or binge drinking) in the prior 30 days, who endorsed at least one DSM-5 substance use disorder criteria in pre-study screening. Substance use was assessed at baseline (N=588), 3 months (N=469) and 6 months (N=476). At each interview, participants were asked whether they used each substance by two methods: (A) semi-structured, clinician-administered interview and (B) computerized self-administered survey (SAQ). Responses using these two methods were then compared using Cohen's Kappa coefficient. Fleiss's procedure assessed differences in agreement by gender, age, race, employment status, marital status and level of education.
Results: Across surveys, there was moderate-to-strong agreement between clinician-administered and self-administered surveys for alcohol (Mean percent difference (MPD) on the SAQ vs. clinician interview=-0.9%, Kappa=0.70–0.88), cannabis (MPD=-0.1%, Kappa=0.87–0.92), cocaine (MPD=0%, Kappa=0.81–0.89), and heroin (MPD=-1.5%, Kappa=0.90–0.92). However, there was weak-to-moderate agreement for non-medical use of prescription painkillers (Kappa=0.55–0.71), with the SAQ capturing a higher prevalence of use (MPD=2.4%). When comparing demographic subgroups, agreement for non-medical use of prescription painkillers was significantly weaker among participants who were aged 40+ (MPD=3.3%,

Kappa=0.48–0.72), unemployed (MPD=2.8%, Kappa=0.52–0.71), non-white (MPD=3.0%, Kappa=0.51–0.73), had lower levels of education (MPD=2.4%, Kappa=0.52–0.67), and were recruited from the community (MPD=3.2%, Kappa=0.48–0.73).
Conclusions: Surveys aimed at measuring non-medical use of prescription painkillers in community samples should consider using self-administered surveys over clinician-administered interviews.
Financial Support: This work was supported by NIDA grant R01DA018652 and by the New York State Psychiatric Institute.

T70. Sex Differences Among Individuals With Chronic Pain and Opioid Use Disorder Entering Methadone Maintenance Treatment

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Although chronic pain (CP) and opioid use disorder (OUD) frequently co-occur, few studies have systematically investigated sex differences among those with CP and OUD. We examined sex differences in demographics and clinical characteristics among individuals with CP (i.e., pain lasting at least 3 months) and OUD entering methadone maintenance treatment (MMT).
Methods: 588 individuals who consecutively entered MMT between April-October 2017 at the APT Foundation, a non-profit community-based organization in Connecticut, completed self-report measures of demographics, CP, and clinical characteristics (i.e., trauma exposure [Life Events Checklist] and psychological distress [Behavior and Symptom Identification Scale]). Among the 338 individuals (57.5%) reporting lifetime CP, we investigated sex differences in demographics and clinical characteristics using a Mann-Whitney-U test for continuous data and Chi-squared test for categorical data. Individuals with a missing variable were dropped for the corresponding test. We controlled for multiple testing using the Benjamini-Hochberg procedure. Data was analyzed in Python.
Results: The 338 participants with CP and OUD ranged in age from 19 to 68 years (M = 38.3, SD = 10.6); 56.8% were men; 81.3% were white; and 11.2% were Hispanic, 165 (48.8%) reported physical assault, and 117 (34.6%) reported sexual assault. Among individuals with CP and OUD, women compared to men reported significantly higher rates of physical assault (60.9% vs. 39.5%, $\chi 2 = 15.2$, $p<.001$), sexual assault (60.9% vs. 14.6%, $\chi 2 = 78.8.18$, $p<.001$) and psychological distress (mean of 1.8 vs. 1.5, AUC=0.59, p=0.02). In pairwise analyses, no significant associations emerged between sex and demographics.
Conclusions: Among individuals with CP and OUD entering MMT, women are more likely than men to report physical assault, sexual assault, and psychological distress. Future studies should assess the potential benefit of developing integrated treatments for OUD, CP, and trauma for individuals (particularly women) entering MMT.
Financial Support: The authors have no conflicts of interest to declare. This research was supported in part by funding from the APT Foundation, Inc, and grants from the NIH/NHLBI/NIDA to Dr. Barry (MPI; U01 HL150596-01 and RM1 DA055310).

T71. Stimulant Use is Strongly Associated With Return to Opioid Use Following Initiation Onto Medications for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Stimulant use among people with opioid use disorder (OUD) is a widespread and growing public health problem which may pose particular challenges to recovery from OUD. We examined how ongoing stimulant use is associated with return to opioid use after initiation onto medication for OUD (MOUD).
Methods: This analysis included 570 participants who initiated buprenorphine or extended-release naltrexone (XR-NTX) in two randomized clinical trials, NIDA CTN 0051 and 0067. Associations between time-varying stimulant use (methamphetamine, amphetamines, or cocaine) and first use of opioids within 180 days of MOUD initiation were estimated using timeline follow-back data and a Cox proportional hazards model. Among participants reporting any opioid use following initiation, logistic regression was used to assess the relationship between stimulant use and a 'severe relapse' – defined as 7 days of continuous opioid use or 4 consecutive weeks in which the participant reported any opioid use, missed a UDT screen, or tested positive for opioids in UDT screen.
Results: Participants averaged 35 years of age, 69% were male, and 66% were white. Forty-seven percent of participants reported stimulant use following MOUD initiation, 58% reported at least one day of opioid use, and 31% reported a severe relapse. Stimulant use was strongly associated with increased risk of return to opioid use after MOUD initiation (aHR=8.4, 95% CI 5.9 to 11.8), with a larger effect ($p = 0.01$) among patients initiating buprenorphine (aHR=12.1, 95% CI 3.4, 9.7) than XR-NTX (aHR=5.8, 95% CI 8.4, 17.8). Among those reporting any opioid use following initiation, using stimulants weekly or more was associated with an increased likelihood of a severe relapse compared to infrequent or no stimulant use (aOR=3.2, 95% CI 1.4, 7.0).
Conclusions: Participants initiated on MOUD who then used stimulants experienced more frequent and more severe return to opioid use compared to non-stimulant users.
Financial Support: NIDA UG1DA015815; NIDA UG1DA013035

T72. TRV734 as a Potential Medication for Opioid-Use Disorder: Protocol for a Dose-Finding Pilot and a Proof-Of-Concept Human Laboratory Study

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Treatment with the opioid agonists buprenorphine and methadone is often effective for opioid use disorder (OUD) but does not eliminate opioid use in all patients. Therefore, there is a need to advance novel medications that are tolerated and efficacious. In humans, intravenous administration of the mu-opioid receptor (MOR) agonist TRV130 decreases moderate-to-severe acute pain and trends towards having fewer side-effects than morphine. In non-human animals, chronic TRV130 delivery decreases relapse to oxycodone seeking in a rat model of opioid maintenance and prevents acute oxycodone-induced brain hypoxia. Here, as an initial proof-of-concept study that may inform future outpatient clinical trials, we will test the effect of TRV734, an orally bioavailable drug with a similar pharmacological profile to TRV130 (oliceridine) on opioid withdrawal suppression among individuals with OUD.
Methods (Optional): After an initial single-blind, dose-finding pilot phase, we will employ a within-subject double-blind placebo-controlled randomized experiment to test whether TRV734 suppresses opioid withdrawal. We will compare TRV734 to placebo and oxycodone. Thirty adults with a DSM-5 diagnosis of OUD and receiving daily methadone treatment will stay at an inpatient unit and undergo four experimental sessions (placebo, oxycodone, and a low and high dose of TRV734) after having two daily methadone doses withheld prior to each session. The primary outcome will be withdrawal suppression, assessed by the Subjective Opioid Withdrawal Scale. Secondary outcomes will include safety, specificity of effects (withdrawal suppression without acute slowing on psychomotor tasks), tolerability, and the objective assessment of withdrawal indicators.
Conclusions: We predict that TRV734 will suppress opioid withdrawal symptoms with fewer side-effects than oxycodone. If proven, this will support advancing long-acting formulations of TRV734 for OUD treatment. Even modest increases in the proportion of patients who are unresponsive to buprenorphine or methadone, but who respond to TRV734, would be a significant public health benefit.

Financial Support: National Institute on Drug Abuse Intramural Research Program

T73. Why Stop a Good Thing? a Qualitative Study of Methadone Discontinuation in the First Year of Treatment for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid use disorder (OUD) treatment with methadone for at least one year reduces all-cause mortality and illicit opioid use, but less than half of individuals remain in methadone treatment at 12 months. The aim of this qualitative study was to explore staff and patient perceptions of why methadone is discontinued in the first year.
Methods: We recruited clinical staff and patients from two opioid treatment programs in Baltimore, Maryland. Patients were eligible for inclusion if their current methadone treatment episode was less than 12 months. We conducted staff focus groups and 60-minute semi-structured individual patient interviews using videoconference calls. Participants were compensated with $30 gift cards. Interviews and focus groups were recorded and transcribed. We used a grounded theory approach with inductive coding to identify emergent themes. Two authors independently analyzed transcripts with regular meetings to iteratively revise codes.
Results: We conducted two staff focus groups of 4-5 participants (nurses, peers, medical providers, and counselors) and four patient interviews from June 1 to December 1, 2021 and will continue interviews until we reach thematic saturation (20-30 interviews expected by March 31, 2022). Three themes emerged and were consistent between interviews and focus groups. First, many patients never intended to continue methadone beyond a few months and conceptualized of methadone as a temporary aid in transitioning from OUD to abstinence. Second, stigma and discrimination played a substantial role in shaping decisions about when to stop methadone. Third, the structure of opioid treatment programs supported some patients and was also burden to some who felt it was not responsive to their stage of recovery.
Conclusions: The decision to stop methadone often reflects a conceptualization of methadone as a short-term intervention. Policies to improve retention should account for this perspective while addressing stigma and adapting clinic structures to different stages of recovery.
Financial Support: This project was supported by the Research in Addiction Medicine Scholars (RAMS) program R25DA033211.

T74. The Influence of COVID-19 on Treatment for Opioid Use Disorder Services in Rural Primary Care Settings: Patients' Perspectives

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: The coronavirus (COVID-19) pandemic influenced how healthcare settings delivered treatment services for opioid use disorder (OUD). We explored perspectives from patients living in rural regions of the United States on the influence of the COVID-19 pandemic on substance use, access to OUD services, and use of telemedicine (TM).
Methods: As part of a larger study, Clinical Trials Network-0102 Rural Expansion of Medication Treatment for Opioid Use Disorder (MOUD), virtual interviews were conducted with patients (n=22) from 12 rural

health care clinics across 7 states (CA, ID, MD, ME, TN, VT, WA) from December 2020 to October 2021. Patients receiving OUD services were asked about how COVID-19 influenced substance use and services delivered to them at these clinics. We conducted content analysis to identify emerging themes. We also asked participants their acceptability of MOUD and TM for MOUD (5-point scale used).
Results: Participants received MOUD for an average of 6 years (M=6.07, SD=5.82), and 86.36% had received some services (primary care or MOUD) through TM. Out of 22 participants, 4 participants indicated they increased their substance use during the COVID-19 pandemic. Content analyses revealed three themes related to COVID-19: 1) minimal influence on substance use behavior; 2) reduced concerns about stigma and experiences of stigma related to OUD when using services delivered through TM; and 3) increased access to mental health services through TM. The average acceptability rating of in-person MOUD and TM-MOUD services was 4.45 (SD=.09) and 4.14 (SD=1.05), respectively.
Conclusions: The impact of COVID-19 on substance use was minimal for patients stable in OUD treatment. The shift towards TM services during the COVID-19 pandemic increased access to mental health services and decreased barriers to OUD treatment (e.g., stigma). Our findings indicate the importance of expanding treatment delivery methods for OUD to meet the needs of rural US residents.
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T75. Trends in COVID-19 Testing, Infection, Vaccination and Housing Assistance Among People Who Inject Drugs in Los Angeles, California and Denver, Colorado During the First Year of the Pandemic

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: To examine trends in COVID-19 infections, testing, and housing by quarter during the first year of the pandemic and to report correlates of COVID-19 infection and vaccination among opioid using people who inject drugs (PWID) in Los Angeles, California, and Denver, Colorado.
Methods: Retrospective survey data was collected from opioid-using PWID between May and November 2021 (n=284). Multivariate logistic regression was used to examine factors with COVID-19 vaccination from April 2020 to March 2021.
Results: The sample was mostly male (76%), white and Latinx (54% and 34% respectively), and unhoused (79%). While all participants used opioids (mostly heroin and fentanyl), methamphetamine use in the last 3 months was reported by 81% and mixing methamphetamine with heroin or fentanyl was reported by 63% of participants. Examined by quarter, recent COVID-19 testing was lower after Apr/June 2020 but returned to nearly 43% by Jan/Mar 2021. Housing assistance declined from 10% in the first observation quarter to 6% in 2021, and COVID-19 infections remained largely the same at 5% in the first and last observation quarters. Ever being COVID-19 infected was associated with being male (Adjusted Odds Ratio[AOR]=11.68; 95% confidence interval [CI]=1.54, 88.82), more frequent injection (less than daily injection versus injected 3 times or more daily, AOR=5.56; 95% CI=1.25, 24.86), and having difficulty meeting needs (AOR=3.94; 95% CI=1.73, 8.96). Receiving a COVID vaccination was associated with prior US armed forces membership (AOR=1.78; 95% CI=1.78, 25.83) and older age (<30, AOR=0.33, 95% CI=0.15, 0.70; 30-39, AOR=0.19, 95% CI=0.10, 0.38; 40-49, AOR=0.27, 95% CI=0.14, 0.55 versus 50 or older).
Conclusions: COVID-19 remained a significant problem for PWID, yet efforts to assist this population have eroded. Efforts to control the COVID-19 pandemic must provide targeted assistance to PWID including better access to housing and medications treatments for opioid use disorder.
Financial Support: NIDA grant #RO1DA046049

T76. Understanding Opportunities and Challenges With Telemedicine-Delivered Buprenorphine During the COVID-19 Pandemic

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Drug Category Opiates/Opioids
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: To understand provider perspectives on buprenorphine care delivery using telemedicine.
Methods: We conducted semi-structured phone interviews with Department of Veterans Health Affairs clinicians at nine VA Medical Centers. Potential study participants were identified as providers who were involved in referrals and provision of buprenorphine treatment for chronic pain and opioid addiction. Each interview lasted approximately 30 minutes. Audio-recordings of all interviews were transcribed and analyzed for major themes related to tele-prescribing practices for buprenorphine.
Results: Twenty-three providers participated in the study, representing 32% of all providers invited to participate. High proportions of participants were psychiatrists (48%) and female (57%). The following four themes were identified: (1) COVID-19 spurred a seismic shift in OUD treatment; (2) Video calls provided a rare window into Veterans' homes and lives; (3) Providers experienced virtual visit challenges including providing care for Veterans who were distracted with other activities during the scheduled appointments and (4) Providers wrestled with paternalism and trust that Veterans would manage with less in-person and toxicology monitoring.
Conclusions: The provider interviews suggested areas in teleprescribing buprenorphine that might profitably be addressed, including clarifying the home or other treatment setting and incorporating it into the treatment, and establishing trust through a medium that can seem distancing.
Financial Support: VA QUERI HX003009 (MIR and mPIs)

T77. Women's Experiences in Injectable Hydromorphone and Diacetylmorphine Treatment Programs in Vancouver, Canada

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Injectable hydromorphone (HDM) and diacetylmorphine (DAM) have recently been expanded in some Canadian settings, but little research has examined women's experiences with these programs. Previous research on addiction treatment has demonstrated how outcomes are gendered and racialized. Factors such as gender power differentials, stigma, and engagement with child welfare systems can contribute to adverse addiction treatment experiences and outcomes. To understand the experiences of women accessing injectable HDM/DAM, this qualitative study drew on concepts of structural vulnerability with specific attention to gender to examine barriers and facilitators to women's engagement in this treatment approach.
Methods: Qualitative interviews were conducted with 16 women enrolled in injectable HDM/DAM and 4 service providers from injectable HDM/DAM programs in Vancouver, Canada. Approximately 50 hours of ethnographic fieldwork was also conducted. Interview transcripts and ethnographic fieldnotes were analyzed thematically in NVivo and by applying intersectional and structural vulnerability frameworks.
Results: Barriers to engagement included constraints on autonomy during treatment, and concerns about surveillance, privacy and safety in the clinic and surrounding area. Despite these barriers, positive relationships with programs staff particularly related to assistance with injection and access to health and social services enabled engagement for some women. Lastly women reported increased control over drug use and income generation activities in daily life due to program engagement lending to decreased gender power differentials in everyday life.
Conclusions: HDM/DAM programs can provide women with increased agency and control over their drug use (e.g., access to safer opioids). However, women face barriers to treatment engagement resulting from gendered power dynamics and stigma (e.g., decreased privacy and autonomy). There is a need for further

research on women's experiences with this treatment and a need for adaptations to the implementation of HDM/DAM programs to meet their needs.
Financial Support: US National Institutes of Health [Grant # R01DA044181; R01DA043408] and a Canadian Institute of Health Research Doctoral Award.

T78. "The Opposite of Addiction is Connection": Syringe Service Program Perspectives on Engaging People Who Use Drugs in Harm Reduction Services During the COVID-19 Pandemic

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Syringe services programs (SSPs) provide critical evidence-based public health services that decrease the risk of infectious diseases, overdose, and other harms from drug use for people who use drugs (PWUD). Many SSPs have experienced evolving COVID-19-related disruptions. We aimed to characterize the impacts of COVID-19 on SSP operations approximately one year into the pandemic.
Methods: A national sample of SSPs completed a semi-structured interview and brief survey evaluating the impacts of COVID-19 on program operations, including financing, service delivery, and care linkages. Qualitative data were analyzed using Rapid Assessment methods, an iterative, approach that identifies a priori and emergent themes. Survey data were analyzed and triangulated with qualitative findings.
Results: 27 SSPs completed study activities between February – April 2021. SSPs described that approaches to syringe distribution have continued to adjust in response to COVID-19, including increases in the use of mobile and home delivery formats and secondary exchanges. SSPs identified multiple barriers that hinder their ability to engage program participants in needed services, including 1) lost connectivity with program participants, 2) limited program resources (e.g., staff, supply, financial) that limit responsiveness to participant needs, 3) reduced capacity to provide HIV/HCV testing and treatment linkages, and 4) changing SUD treatment modalities that exacerbate PWUD disengagement and disparities. Quantitative survey data echoed that compared to pre and early COVID-19 periods, SSPs are currently experiencing increases in the number of syringes distributed, more mobile and home delivery services, and reductions in HIV and HCV testing.
Conclusions: Data from this study characterize how COVID-19 influences SSPs' abilities to deliver harm reduction services one year into the pandemic, and the challenges SSPs are currently navigating when trying to establish supportive connections with PWUD, an essential component of harm reduction service delivery. These data illuminate potential long-term impacts on PWUD health and well-being as COVID-19 continues to evolve.
Financial Support: This work was supported by the National Institute on Drug Abuse (R01 DA027379 and P30DA040500).

T79. A Pilot Randomized Clinical Trial Examining Buspirone as an Adjunctive Medication During Buprenorphine-Assisted Supervised Opioid Withdrawal

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Successfully managing opioid withdrawal during the treatment of opioid use disorder (OUD) improves long-term treatment outcomes and consequently reduces opioid-related morbidity and mortality. This double-blind, placebo-controlled, randomized pilot trial examines the efficacy of buspirone, a D2 antagonist and 5-HT1a agonist, to mitigate acute and protracted opioid withdrawal.
Methods: Fifteen individuals in residential treatment for OUD and undergoing an 8-day buprenorphine taper were randomized to receive placebo or buspirone in addition to standard care. Those assigned to buspirone underwent an initial 4-day titration then received 45mg/day of buspirone until discharged from residential treatment. Residential treatment lasted no more than 28 days. Participants completed the Subjective Opiate Withdrawal Scale (SOWS) daily. SOWS scores were compared between treatment groups (Placebo and Buspirone) and over time (Day) in a repeated-measures linear mixed model. In a separate model, time was coded into three phases: (1) 4-day buspirone titration, (2) week 1 of stable medication and (3) week 2 of stable medication, to explore the impact of buspirone on acute withdrawal (days after buprenorphine tapering), and protracted withdrawal (1 week after buprenorphine tapering ended).
Results: SOWS scores (withdrawal) decreased in severity over study days in both groups, but persons assigned to buspirone reported lower withdrawal scores relative to those who received placebo after the 4-day titration; group X day interaction, $p = .02$. Significant differences in SOWS scores were observed between treatment groups during week 1 (Buspirone M = 10.2, SEM = 3.1, Placebo M = 14.5, SEM = 4.3) and 2 (Buspirone M = 4.8, SEM = 1.8, Placebo M = 11.1, SEM = 4.0), but not during titration; group X phase interaction, $p < .001$.
Conclusions: Buspirone may help mitigate opioid withdrawal during a supervised opioid taper and may confer unique and greater benefits during protracted withdrawal periods (i.e., 1 week after taper).
Financial Support: Dalio Philanthropies, T32 DA007209

T80. A Randomized Controlled Trial of an Online Training to Reduce Primary Care Clinicians' Stigma Toward People With Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Many primary care clinicians (PCCs) hold stigma towards people with opioid use disorder (OUD), which may be a barrier to care. Few interventions exist to address PCC stigma toward people with OUD. The purpose of this study was to examine whether an online training incorporating patient narratives reduced PCCs' stigma toward people with OUD and increased intentions to treat people with OUD compared to an attention-control training.
Methods: PCCs from 15 primary care clinics were invited to complete a 30-minute online training for an electronic health record embedded clinical decision support (CDS) tool that alerts PCCs to screen, diagnose, and treat people with OUD. PCCs were randomized to receive a stigma-reduction version of the training with patient narrative videos or a control training without patient narratives. Immediately after the training, PCCs completed surveys of stigma towards people with OUD and intentions to get waivered to prescribe buprenorphine or prescribe buprenorphine if a waiver were no longer required. Analyses included independent samples t-tests and Pearson correlations.
Results: A total of 88 PCCs (58% female; 68% white; 67% MD/DO, 33% PA or NP) completed the training (Stigma=48; Control=40). There was no significant difference between intervention and control groups on stigma ($t=-0.48$, $p=.64$, Cohen's $d=-0.11$), intention to get waivered ($t=1.11$, $p=.27$, $d=.26$), or intention to prescribe buprenorphine if a waiver was no longer required ($t=0.90$, $p=.37$, $d=.21$). PCCs who reported greater stigma also reported lower intentions to get waivered ($r=-.25$, $p=.03$) and to prescribe buprenorphine with no waiver ($r=-.25$, $p=.03$).
Conclusions: Stigma towards people with OUD may require more robust intervention than this brief training was able to accomplish. However, stigma was related to lower intentions to treat people with OUD, suggesting stigma acts as a barrier to care. Future work should identify effective interventions to reduce stigma among PCCs.
Financial Support: This work was supported by a HEAL supplement to NIDA CTN 0095 under grant UG1DA040316.

T81. Analyzing Whether Social-Emotional Resources Attenuate the Relationship Between Adverse Childhood Experiences and Opioid Misuse Among Justice-Involved Adolescents

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid misuse among justice-involved adolescents can result in a plethora of adverse life outcomes that can continue into adulthood, including recidivism, overdose, and death. Identifying the key protective and risk factors is crucial to developing programs to prevent or treat opioid misuse. Adverse childhood experiences (ACEs) scores, one of the most renowned and widely used measures of childhood trauma, have been identified as a risk factor for opioid misuse. Social-emotional learning has flourished in recent years as an effective method to foster resilience to trauma and other risk factors. The stress process theory submits that resources can buffer the impact of stressors. This current study was the first to investigate whether social-emotional resources attenuate the effects of ACEs on the odds of opioid misuse specific among justice-involved adolescents in Florida.
Methods: Stepwise logistic regression was employed to analyze a state-level representative sample of over 100,000 JIA from the Florida Department of Juvenile Justice. This sample represents all youth who were arrested, completed the full intake assessment, and reached 18 years old by 2016. The variables measuring past 30-day opioid misuse and social-emotional resources were derived from self-reported data.
Results: Over 90% of the sample had experienced at least one ACE item. ACEs had a dose-response pattern with the odds of opioid misuse. Experiencing one additional ACE was associated with 36% higher odds of opioid misuse. Social-emotional resources had a stronger association with opioid misuse and reduced the impact of ACEs by nearly 40%.
Conclusions: The results of this study corroborated social-emotional learning as a method to reduce the risk for opioid misuse among vulnerable adolescents. Efforts to expand social-emotional learning may bolster efforts to address the opioid misuse crisis.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

T82. Best Practices for Drug Testing During Medication for Opioid Use Disorder (MOUD) Treatment Over Telemedicine

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Provision of medication for opioid use disorder (MOUD) via telemedicine has increased treatment access among individuals with opioid use disorders. Urine toxicology is commonly used to measure MOUD adherence, yet no universal standard exists for drug testing during MOUD therapy, especially through telehealth. The aim of this study was to explore clinicians' perspectives on best practices for drug testing when prescribing MOUD through telemedicine, as well as patients' views on the impact of this practice.
Methods: We conducted thematic analysis from key informant interviews of 27 healthcare providers, including prescribers, substance use counselors, and nurses who utilized telemedicine for MOUD management and 20 patients receiving MOUD through telemedicine. Patients and healthcare providers were recruited from drug treatment facilities, primary care clinics, and low-threshold buprenorphine sites.
Results: Healthcare providers universally agreed on the clinical utility of a baseline test and the importance of subsequent education about precipitated withdrawal in the circumstance of a fentanyl-positive result.

Urine specimens continued to be collected as providers shifted to telemedicine, though less frequently. Providers emphasized that toxicology screens were not used punitively but rather to help them understand patients' unique needs. Many providers emphasized the patient-provider relationship and open communication to determine patients' MOUD adherence. Patients shared that drug testing was an acceptable practice, reporting that urine collection occurred with varied frequencies when using telehealth. Delivering urine specimens to a lab for testing created a barrier to care. However, some saw urine toxicology as a source of accountability, supporting their recovery. Many patients also reported open communication regarding substance use with their providers regardless of drug testing.
Conclusions: Overall, patients and healthcare providers discussed the utility of urine toxicology even when conducting MOUD treatment over telemedicine, but as one of many tools to assess adherence, emphasizing a strong patient-provider relationship.
Financial Support: Bloomberg American Health Initiative and NIDA Drug Dependence Epidemiology T32

T83. Buprenorphine Misuse in Opioid Use Disorders: Subgroups, Motivations, and Opioid Demand

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Drug Category Opiates/Opioids
Topic Behavioral Economics
Abstract Detail Human
Abstract Category Original Research
Aim: We sought to classify reasons for buprenorphine misuse between the first and most recent occurrence, and to assess behavioral economics of the different types of misuse among individuals with reported past or current Opioid Use Disorder (OUD).
Methods: Individuals (n=302) with a history of OUD completed a survey, including reasons for buprenorphine misuse; the 5-trial delay discounting task; and an opioid/buprenorphine purchase task. Subgroups with similar motivations for buprenorphine misuse were identified using k-means. Buprenorphine demand and preferred opioid demand characteristics were compared among subgroups using ANOVA.
Results: Respondents were an average of 38 years old, majority male (58.9%), and Caucasian/White (84.8%). Four subgroups were named based on themes of reasons for misuse: Dependence, Ambivalence, Harm Reduction, and Substitution. For most recent misuse, significant differences in demand intensity (Q0) for preferred opioid ($p= 0.010$) and buprenorphine ($p=0.026$) were found among subgroups; those misusing for Dependence have higher Q0 for buprenorphine and opioids compared to all other subgroups. No differences in demand elasticity (alpha) for preferred opioid ($p=0.403$) or demand elasticity (alpha) for buprenorphine ($p=0.104$) among subgroups were observed. The reasons grouped with Substitution/Dependence demonstrate a pattern of sustained opioid use; Harm Reduction corresponds to reduced use of other opioids; Ambivalence has minimal association with any reasons for misuse. Those who initially misuse buprenorphine for Substitution/Dependence transition to the Harm Reduction/Ambivalence at a rate of 69.79%, while the opposite had a conversion rate of 3.88%.
Conclusions: This study indicates that people with OUD who misuse buprenorphine have variable motivations for misuse, which can change over time. Those misusing for Dependence have a higher demand intensity (Q0) for buprenorphine and opioids compared to all other subgroups. Our results indicate that those who initially misuse buprenorphine with Dependence/Substitution motivations will likely have different motivations for their most recent misuse of buprenorphine.
Financial Support: Indivior, Inc.

T84. Changes In Substance Use Behaviors Among Those Who Use Opioid Analgesics

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human

Abstract Category Original Research
Aim: Though opioid analgesic prescriptions decreased 17% (IQVIATM US-Based Longitudinal Prescription Data) between 2018 and 2020, deaths involving natural or semisynthetic opioids were stable. To examine reasons for this divergence, we analyzed substance use behaviors among adults reporting past year use of opioid analgesics.
Methods: The Survey of Non-Medical Use of Prescription Drugs Program is a semiannual online panel-based general population survey of adults in the United States. Each respondent completes a questionnaire asking about the use and misuse of prescription and illicit drugs. We assessed problematic substance use with Drug Abuse Screening Test (DAST-10) scores and nonprescription fentanyl (NPF) use among respondents who reported past year use of hydrocodone, hydromorphone, morphine, oxycodone, or oxymorphone across seven survey launches conducted between September 2018 through September 2021. Calibration weighting was used to create nationally representative estimates. Generalized linear mixed models were used to estimate prevalence and changes across launches.
Results: The number of adults who used prescription opioid analgesics in the past year decreased from 45.8 (95% CI: 44.7-46.9) million in September 2018 to 40.4 (95% CI: 39.2-41.5) million in September 2021. However, the number who had problematic substance use in the past year (endorsed 4+ DAST-10 items) remained consistent, 3.9 (95% CI: 3.6-4.2) million in 2018 and 4.0 (95% CI: 3.7-4.4) million in 2021. The number of PO using adults who also reported past year use of NPF increased (0.5 million to 0.9 million). Most respondents (57%) who used NPF in the past year in the general population also reported use of a prescription opioid analgesic in the past year.
Conclusions: Despite declines in the number of adults who use prescription opioids, the number of adults with problematic substance use who use prescription opioids have remained unchanged. A small but increasing number of adults who report use prescription opioids also report use of NPF.
Financial Support: The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado. The RADARS System is supported by subscriptions from pharmaceutical manufacturers, government and non-government agencies for surveillance, research and reporting services. Subscribers did not participate in data collection or analysis this abstract. Direct funding for this study was provided by the Denver Health and Hospital Authority.

T85. City Streetscapes and Neighborhood Profiles of Fatal Opioid Overdoses Among Unstably-Housed People Who Use Drugs

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: While housing is a critical social determinant of nonprescription opioid overdose, little is known about how place impacts fatal overdose for people who use drugs (PWUD) experiencing homelessness or unstable housing. This study examines patterns in built environment features at locations of fatal overdoses among unstably-housed PWUD.
Methods: We remotely visited locations of opioid-involved fatal overdoses provided by the New York City Office of the Chief Medical Examiner, 2017-2019 (n=3,267), with Google Street View and used a reliable and valid tool to assess characteristics of the street block related to drug exposures. We cross-referenced home address with city shelters and supportive housing to identify PWUD experiencing homelessness or unstable housing (n=503). We used the differences of K functions from the spatial point patterns and kernel intensity function to test for significant global clustering and logistic regression to test significant individual-, block-, and neighborhood-level covariates.
Results: Over half of fatal overdoses among unstably-housed PWUD occurred in supportive housing or shelters (n=272), and 16.8% occurred in public spaces (e.g., parks, restaurants) (n=85). Spatial point pattern analyses comparing unstable versus stably-housed PWUD identified areas of concentrated fatal overdoses among unstably-housed PWUD. Unstably-housed PWUD were significantly more likely ($p<0.05$) to overdose on blocks with bars, abandoned buildings, graffiti, new construction, and visible police presence, and significantly less likely to overdose on blocks with game courts (e.g., basketball courts), public benches

not associated with bus stops or parks, traffic calming infrastructure (e.g., speed bumps), and adults doing yard work (controlling for neighborhood-level income, segregation, and population density indicators).
Conclusions: While supportive housing is a necessary step in preventing fatal opioid overdoses, identifying new avenues and community profiles for intervention services delivery and harm reduction outreach is necessary. Harm reduction services should be co-located in facilities that serve unstably-housed PWUD and targeted to blocks with indicators of disorder.
Financial Support: National Institute on Drug Abuse (grant number K01DA049900)

T86. Enhancing Social Determinants of Health Among People With Opioid Use Disorder on Buprenorphine

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Social Determinants of Health (SDOH) are critical elements related to an individual's health and may have an impact on treatment outcomes among patients with opioid use disorder (OUD). While buprenorphine is an effective medication for OUD, SDOH may impede its effectiveness. Here we tested the impact of an intervention combining CBT4CBT and recovery coaching (CBT4CBT+RC) vs. treatment as usual (TAU) on SDOH in a sample of persons receiving buprenorphine.
Methods: 30 participants with OUD on buprenorphine were randomized to 8 weeks of the integrated intervention combining CBT4CBT+recovery coaching or a TAU condition. SDOH was evaluated with the self-sufficiency matrix, which assesses deficits in the following domains: housing, employment, income, food, childcare/children education, education, health care, life skills, family/social relationships, mobility, parenting skills, legal, mental health, substance use, safety, and disabilities. Each domain is rated on a Likert scale from 1 to 4, with greater scores indicating better SOH.
Results: All participants (43.3% female, Mage= 39.6) reported drug use in the 30 days before enrollment. Toxicology screens verified that the most commonly used drugs were methamphetamine (27.6%), amphetamine (20.7%), and THC (20.7%). At baseline, participants had an average total score of 52.6 in the self-sufficiency matrix, with no differences between groups (52.7 CBT4CBT+RC vs 52.6 TAU). At the end of treatment, we found significantly greater improvements in the CBT4BT+RC group than the TAU group in the total score (56.8 vs. 46.6;p=.018) as well as in the domains of mental health (3.9 vs. 3.5;p=.004), substance use (4.3 vs. 3.1;p=.011), and safety (4.5 vs 3.1;p=.014).
Conclusions: The integrated intervention combining CBT4CBT and recovery coaching resulted in improvements in overall SDOH as well as in the specific domains of mental health, substance use, and safety. Delivering interventions that simultaneously address SDOH and OUD maintenance treatment has the potential to reduce SDOH disparities among people with OUD
Financial Support: Health Sciences Center at Prisma Health Transformative Research Seed Grant Award

T87. Experiences With Treatment for Opioid Use Disorder and Substance Use During the COVID-19 Pandemic Among People Who Use Opioids: A Web-Based Survey

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid overdose deaths have increased nationwide during the COVID-19 pandemic. Exploring how changes to opioid use disorder (OUD) treatment and variations in drug supply may impact people who use

opioids is critical. This survey aimed to gain insight into the experiences of people who use opioids and investigate the impacts on OUD treatment and substance use during the COVID-19 pandemic.
Methods: Experiences with treatment and substance use were assessed through an online Qualtrics survey. Participants (n=182) were recruited in April 2021 through Reddit forums. Eligible participants were 18 years of age or older, resided in the United States, and scored a three or higher on the Rapid Opioid Dependence Screener (RODS). Descriptive statistics were calculated using Stata.
Results: Since January 1, 2020, 66.1% (n=111) of participants engaged in OUD treatment. Seventy-seven percent of these participants (n=86) reported stopping or taking a break from treatment due to family (n=42, 48.8%), transportation (n=29. 33.7%), and financial-related (n=23. 26.7%) challenges. Among participants prescribed medication for OUD (MOUD; n=101, 55.4%), 51.5% (n=52) engaged in virtual/telehealth treatment. Perceptions of telehealth treatment were largely positive, with 45.5% (n=46) of participants preferring telehealth to in-person appointments. A majority of the sample reported increased use of opioids (n=97, 53.3%), other non-prescribed drugs (n=74, 40.7%), and cannabis (n=71, 39.0%). Despite reports of increased substance use, participants generally endorsed increased difficulty (n=67, 51.5%) finding drugs in the community.
Conclusions: The COVID-19 pandemic amplified barriers to OUD treatment that substantially impacted treatment continuity even as telehealth became more accessible. In combination with reports of increased substance use, study findings support the urgent need for interventions addressing family (e.g., childcare), transportation, and financial barriers.
Financial Support: NIDA P30 DA029926

T88. Federal Policy Changes and Buprenorphine Treatment Capacity in the US: An Interrupted Time Series Analysis

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: In response to the ongoing US opioid epidemic, federal policies have evolved over time to allow physicians to treat more patients with buprenorphine and to expand buprenorphine prescribing to additional medical professions, such as nurse practitioners (NPs) and physician assistants (PAs). The present study examines the impacts of these two policy changes on buprenorphine treatment capacity.
Methods: Monthly counts of all US waivers were extracted from the DEA's Controlled Substances Act (CSA) Active Registrants database from June 2013 to May 2018. Waiver counts were multiplied each month by their respective patient limits (30, 100, 275) and then summed to measure monthly buprenorphine treatment capacity, meaning the total number of patients who could be treated. Interrupted time series analysis was used to examine changes in buprenorphine treatment capacity after the implementation of the 275-patient physician waiver and after the implementation of waivers for NPs and PAs. Physicians with the 275-patient waiver first appeared in September 2016, and the first NPs and PAs appeared in April 2017.
Results: Over the five-year period, US buprenorphine treatment capacity (BTC) increased from 1.1 million to 3.0 million. Prior to the 275-patient waiver, BTC was increasing at a rate of 13,627 per month (95% CI: 13,265, 13,988; p<.001). Following the 275-patient waiver, the trend increased by 75,524 per month (95% CI: 43,461, 107,587; p<.001), for a post-implementation linear trend of 89,151 (95% CI: 57,021, 121,280). The NP/PA waiver in April 2017 reduced the trend in BTC relative to the post-275 waiver trend (coefficient=-37,485, 95% CI: -69,773, -5,197, p=.02), but the monthly post-implementation linear trend continued to be positive (coefficient=51,666, 95% CI: 49,803, 53,528, p<.001).
Conclusions: Although both policies increased capacity, the 275-patient waiver had a larger impact than the NP/PA waiver in expanding buprenorphine treatment capacity.
Financial Support: Supported by the National Institute on Drug Abuse (R33DA035641).

T89. Gabapentin Levels Impact on Successful Transition to Injectable Naltrexone

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Gabapentin (GBP), well tolerated/effective in reducing craving/opioid use in pilot detoxification trials. We previously reported medication group (GBP versus placebo) did not predict outpatient transition to oral/naltrexone injection (NTXI) in randomized, placebo-controlled trial. The present study determined if GBP blood levels (BL) were associated with transition from BUP to NTX.
Methods: Data obtained from 53 participants starting week4 in randomized, placebo-controlled trial to determine utility of adjunct GBP in opioid-dependent individuals undergoing outpatient BUP detoxification and feasibility of transitioning to NTXI. During weeks1-3, participants attended clinic 5-6 days/week to receive study medications, attend weekly therapy and complete assessments. Participants were inducted onto 12 mg buprenorphine daily by day2, week1 and randomized to placebo or GBP (800 mg BID) day3, week1. Ten day BUP taper started day3, week2 with 1 mg days 4/5 week3. Participants returned day1 week4 for 4-day oral NTX induction followed by NTXI day5. GBP BL obtained day1, week4. Participants with opioid-negative UDS received clonidine, followed by oral NTX.
Results: Fifty-three participants entered week4. No significant differences between placebo/GBP occurred in receiving oral or first NTXI (previously presented). Of those with low (0-199 ng/ml), intermediate (200-2000 ng/ml) and high (>2000 ng/ml) GBP BL, 64%, 25% and 68.8% received oral NTX on day1 ($p=0.05$). No differences in receiving week4 NTXI (low 52% vs. intermediate 33.3% vs. high 43.8%; $p=0.65$). Of those that received week 4 NTXI, 16.7% with no GBP vs. 66.7% with some GBP received week8 NTXI ($p<0.02$).
Conclusions: GBP blood levels did not predict successful transition to oral or first injection NTX, although trends with low and high levels of GBP being associated with receiving initial oral naltrexone and any GBP blood level being significantly associated with receiving the week 8 NTX injection suggest more work may be necessary to elucidate impact of GBP blood levels on depot NTX compliance.
Financial Support: This work is supported by NIDA grant R01DA036544-01A1 and authors have no disclosures.

T90. Impact of Telemedicine on Retention in Medications for Opioid Use Disorder (MOUD) Treatment With Buprenorphine in the Times of COVID-19 Pandemic: A Retrospective Chart Review

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: This study reviewed the impact of telemedicine on treatment retention in Medication for Opioid Use Disorder (MOUD) with buprenorphine treatment program during the COVID-19 pandemic.
Methods: Electronic health records of active patients (both sexes) in MOUD with buprenorphine treatment program were reviewed from July 1, 2019, to June 30, 2020. Data were divided into four groups of three-months' time points to calculate and compare treatment retention in the baseline, Pre-COVID, and In-COVID groups. Total numbers of active patients identified in the study's four groups were 309, 327, 360, and 365 respectively. he percentage of treatment retention with a 95% confidence interval was calculated using UCSF-CTSI sample size calculator tool.
Results: The numbers of patients retained in treatment in consecutive groups of three-months' time points are 286, 308 and 327. The percentage of patients retained in treatment in consecutive groups of three-months' time points are 92.55%, 94.18%, and 90.83% with the 95% confidence intervals of treatment retention being [0.896, 0.956]; [0.916, 0.967]; [0.878, 0.938] respectively.
Conclusions: This study presents data suggesting that telemedicine is efficacious in retaining patients in MOUD. Telemedicine is an alternative to face-to-face treatment delivery for MOUD with buprenorphine treatment. It should be available to provide services after the pandemic as well.

T91. Naloxone Provision and Overdose Prevention Education for Patients with Opioid Use Disorder in Four Urban Emergency Departments

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: We sought to evaluate the frequency of naloxone provision and overdose prevention education among emergency department (ED) patients with opioid use disorder (OUD) and to determine if it differed based on ED visit for OOD compared to other chief complaints.
Methods: Between Feb 2017 and Dec 2020, ED patients with untreated OUD were enrolled in Project ED Health, a NIDA CTN, Hybrid Type 3 implementation-effectiveness study to promote ED-initiated buprenorphine at 4 urban, academic sites in Maryland, New York, Ohio and Washington. For this analysis, we categorized OOD visits based on ICD-10 codes and/or chief complaint and used participant-provided gender, race, ethnicity, housing status, and past 30-day OOD in addition to ED visit data including ICD-10 codes, chief complaint, provision of take-home naloxone (THN), naloxone prescription, and documented overdose prevention education. Outcomes were evaluated using descriptive statistics, multi-variate regressions, and Chi-Square tests.
Results: Among 756 patients, 103 (13.6%) presented with OOD at the index ED visit. No significant differences in gender, race, ethnicity, housing instability between patients enrolled with vs. without OOD were found. Among 756 patients, 36/756(4.8%) were dispensed THN and 72/756(9.5%) received a naloxone prescription; only 58/756(7.7%) received overdose prevention education. Patients with OOD were more likely to be provided THN (6/103(5.8%) vs 12/653(1.8%); $p<0.001$), receive a naloxone prescription (29/103(28.2%) vs 25/653(3.8%); $p<0.001$), or to receive overdose prevention education (25/103(24.3%) vs 33/653(5.1%); $p<0.001$.) Among patients with OOD, 84/103 (81.2%) reported one or more and 10/103 (9.7%) reported two or more OODs during 30 days prior to study enrollment.
Conclusions: Patients presenting after OOD were more likely to receive THN or be prescribed naloxone than those presenting for other reasons. However, the overall rates of these life-saving interventions were very low. Strategies to enhance the provision of home naloxone, overdose prevention education and treatment among ED patients with OUD are urgently needed.
Financial Support: 5UG1DA015831-15

T92. OPENing Hearts and Minds: Lessons Learned in the Implementation and Facilitation of a Weekly Online Opioid Use Disorder Educational Series

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Program Descriptions
Aim: The Kentucky Opioid Prevention Education Network (KY-OPEN) is a weekly online-based educational series designed to provide healthcare professionals, peer support specialists, and community stakeholders with foundational and emerging knowledge regarding opioid overdose prevention and Opioid Use Disorder (OUD) management. As part of the Kentucky HEALing Communities Study, the sessions create a forum for sharing program developments and implementation strategies to meet the needs of the communities the study serves.
Methods (Optional): Prior to launch, we collaborated with Medication for Opioid Use Disorder (MOUD) providers, organizations that link and retain persons on MOUD in care, and community stakeholders in participating counties to cultivate an initial audience and list of OUD management and overdose prevention

topics. Additionally, continuing education was obtained for multiple disciplines (i.e., nursing, physicians, pharmacists, peer support specialists, social workers). To support engagement, we developed a weekly newsletter that provides content related to session activities, local programming, and information related to OUD and MOUD.
Results (Optional): In 2021, KY-OPEN held 47 sessions with 18 different speakers, covering a range of topics including overview of substance use disorders, MOUD and stigma, common co-morbidities and treatment in special populations (e.g., pregnancy). Average attendance at live sessions was 23 individuals, with over 1000 total participants and 147 unique participants. Session recordings have over 1000 views and over 300 hours of watch time. 172 individuals claimed CME or CE credit. Overall, feedback has been positive. Participants indicated the knowledge and/or skills gained from activities will improve their ability to support people living with OUD.
Conclusions: KY-OPEN represents a coordinated effort to provide community support and education for multidisciplinary professionals in Kentucky to learn more about treatment for OUD. While there is significant effort required to plan and deliver this program, implementation data suggest that it has been successful in engaging with the community and delivering valuable educational content.
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T93. Opioid Knowledge Test: Identifying Knowledge Gaps Regarding Opioids Among College Students, Researchers, and Treatment Providers

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Drug Category Opiates/Opioids
Topic Prevention
Abstract Detail Human
Abstract Category Original Research
Aim: The prevalence of opioid use disorder and rates of opioid overdose in the United States have increased significantly over the past 20 years. Given this increase and increased media attention on the "opioid epidemic", it stands to reason that most individuals have formed opinions and beliefs about opioids and about people who use opioids. To identify potential knowledge gaps regarding opioids, we developed the Opioid Knowledge Test.
Methods: We conducted two studies to examine opioid knowledge among distinct populations. Study 1 recruited college students across 10 universities in the United States (n = 2,518, 71.3% female). Study 2 recruited participants (n = 243, 58.8% female) from several distinct populations including researchers (n = 163) and treatment providers (n = 80) to complete the knowledge test.
Results: On average, participants in Study 1 and 2 correctly answered 37.1% and 52.3% of our items, respectively. For Study 1, the lowest and highest levels of accuracy on an item were about treatment options (8.0%) and addictive potential (67.3%). For study 2, the lowest and highest levels of accuracy on an item were about comorbidity (25.3%) and opioid withdrawal (74.1%). Although opioid researchers and those providing treatment to individuals with opioid use disorder outperformed non-opioid researchers and treatment providers on the overall knowledge test, we did not find significant group differences on most items, demonstrating that some of these knowledge gaps exist across subpopulations.
Conclusions: The Opioid Knowledge Test highlights important knowledge gaps about opioids among researchers, treatment providers, and others with important implications for education, prevention, treatment, and policy surrounding opioids. Educational efforts designed to minimize knowledge gaps may be helpful and potentially protective for many populations.
Financial Support: Research funding provided by the University of New Mexico-Substance Use Disorders Grand Challenge. FJS is supported by the National Institute on Alcohol Abuse and Alcoholism (T32 AA018108).

T94. Open Board

T95. Effects of Dimethylfumarate on Morphine Withdrawal Symptoms and In Vivo Neurochemistry in Morphine-Dependent Mice: A Behavioral and Proton Magnetic Resonance Spectroscopy Study

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Drug Category Opiates/Opioids
Topic Tolerance/Dependence
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Over 70,000 deaths in the US this past year were attributable to opioids and most occurred in people with opioid use disorder (OUD). A better understanding of opioid withdrawal symptoms, which perpetuate OUD and are driven in part by inflammation, could lead to better treatments that reduce morbidity and mortality. In morphine-dependent mice, we tested whether the potent anti-inflammatory agent dimethylfumarate (DMF) alters morphine withdrawal symptoms and neurochemistry, assessed with in vivo magnetic resonance spectroscopy (MRS).
Methods: Adult CD-1 mice (12-15/sex) received twice daily oral DMF (50 mg/kg, p.o.) or vehicle (3% carboxymethylcellulose) followed by twice daily morphine injections (20 mg/kg, s.c.) for 10 days to induce morphine dependence. On day 9, these mice and untreated control mice (8/sex) underwent isoflurane (1-2%)-anesthetized 9.4 Tesla MRS scans of medial frontal cortex (MFC) and striatum (Str). On day 10, four hours after the last morphine+DMF/vehicle doses, naltrexone (1 mg/kg, s.c.) was given to precipitate withdrawal symptoms, and behaviors were videorecorded for 45 minutes. MRS spectra and behaviors were analyzed in a blind manner. Two-way (treatment, sex) ANOVAs were used for statistical analyses.
Results: Morphine dependence was associated with increased MRS glutamate and decreased MRS taurine levels in MFC and Str; moreover, taurine was reduced to a greater extent in females (all Ps<0.04). In males but not females, DMF normalized taurine levels and attenuated naltrexone-precipitated jumping behavior.
Conclusions: Morphine dependence increased glutamate and decreased taurine levels in mice and DMF normalized taurine levels in males. Since taurine inhibits glutamate neurotransmission and attenuates sympathetic nervous system activity and gut leakiness, drivers of opioid withdrawal symptom severity, DMF's beneficial effects in males could result from its enhancement of taurine levels. Like DMF, taurine has anti-inflammatory effects that also could reduce morphine withdrawal symptoms. Our data suggest that DMF, taurine, or their analogs could reduce opioid withdrawal symptoms.
Financial Support: NIH grants U18DA052344 and S10RR019356 and United States/Army Contracting Agency Contract Number DABK39-03-C-0075 from the Counter-Drug Technology Assessment Center (CTAC), an office within the Office of National Drug Control Policy (ONDCP).

T96. Analysis of Stimulant Prescriptions, Drug-Related Poisonings, and Treatment Retention Among Patients Receiving Buprenorphine for Opioid Use Disorder.

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Prescription stimulant use among persons with opioid use disorder (OUD) has been understudied. We examined whether prescription stimulant use was associated with risk of (1) drug-related poisoning (DRP) and (2) attrition from buprenorphine treatment among persons with OUD.
Methods: We used a retrospective case-crossover cohort study design to analyze administrative claims data from IBM® MarketScan® Commercial and Multi-State Medicaid Databases from January 1, 2006 to December 31, 2016. Our sample included males and females with an OUD diagnosis aged 12-64 prescribed

buprenorphine and who experienced at least one DRP. Our unit of observation was person-day; there were 12,623,967 person-days of observation among n=20,367 individuals. We used conditional logistic regression to measure associations between active stimulant prescription days and likelihood of (1) DRP and (2) buprenorphine treatment attrition. DRPs were defined using International Classification of Diseases-9 and -10 codes; buprenorphine treatment attrition was defined as at least 45 consecutive days without an active buprenorphine prescription.
Results: Relative to no treatment, stimulant treatment days were associated with increased DRP risk (odds ratio [OR]: 1.20, 95% CI: 1.03-1.39) and buprenorphine treatment days were associated with decreased DRP risk (OR: 0.70, 95% CI: 0.66-0.75). No interaction effects were observed. Stimulant treatment days were associated with decreased risk of buprenorphine treatment attrition (OR: 0.59, 95% CI: 0.53-0.64), illustrating mean duration of exposure to buprenorphine was approximately 40% longer for individuals prescribed stimulants compared to those who were not.
Conclusions: Among persons with OUD who experienced a DRP, prescription stimulant use was associated with a modest increase in risk of DRP, but this risk may be offset by the association between stimulant use and improved retention to buprenorphine, which protects against overdose. Our findings highlight the complicated risk-benefit ratio clinicians must weigh when treating persons with OUD and co-occurring conditions for which stimulant use is indicated.
Financial Support: This project was supported by the following: K12DA041449-03 (CMM, LJB); R25 MH112473-01 (KYX); R21 DA04744 (RAG, NJP); Saint Louis University Research Institute (RAG); R21 AA024888 (SMH), R01 AA029308 (SMH), K24 DA029647 (FRL), SAMHSA H79TI082566 (CMM, SMH). This project was supported by the Washington University Institute of Clinical and Translational Sciences grant UL1 TR002345 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health, as well as the Center for Administrative Data Research at Washington University which receives support from UL1 TR002345 and from R24 HS19455 through the Agency for Healthcare Research and Quality (AHRQ).

T97. Transcriptomic Hallmarks of Genetic Knockdown of the 5-HT2A Receptor in Rat Medial Prefrontal Cortex: Implications for Understanding Psychedelic Actions

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Drug Category Psychedelics
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Transmission via the 5-HT2A receptor (5-HT2AR) in the medial prefrontal cortex (mPFC) is implicated in neuropsychological disorders and the actions of serotonergic psychedelics. Doses of psychedelics that evoke 5-HT2AR-mediated head twitches in rodents correlate to doses that evoke hallucinations in humans (Psychopharmacologia 11:65, 1967). Indeed, intra-mPFC microinfusion of an hallucinogen was sufficient to generate head twitches which were blocked by a selective 5-HT2AR antagonist (JPET 282:699, 1997). Here, we engineered a viral vector to knockdown the 5-HT2AR in the mPFC of adult rats to investigate how 5-HT2AR deficiency affects the transcriptional profile of mPFC neurons.
Methods: A short hairpin RNA (shRNA) that knocks down 5-HT2AR in vitro or a non-silencing control (NSC) shRNA was packaged into an adeno-associated viral (AAV2) vector, purified and assayed to confirm titers of 1 × 1012-13 transducing units/mL. Naïve male Sprague-Dawley rats received bilateral intra-mPFC infusions of each viral vector and were allowed to recover for three weeks to allow for stable transgene expression, followed by extraction of the mPFC for RNA-seq analysis.
Results: The transcriptomic analysis revealed that 5-HT2AR knockdown was sufficient to induce dramatic changes in gene expression in mPFC identifying HTR2A as a master regulator of a causal network of genes centered around EGFR as well as genes mediating glutamate and GABA synaptic homeostasis (e.g., GAD1, GAD2, EAAT3, SLC1A1). In total, n = 1132 genes of interest exhibited a Benjamini-Hochberg adjusted $p < 0.01$; n = 686 gene transcripts were higher while n = 446 were lower in the mPFC of 5-HT2AR knockdown vs. control rats.

Conclusions: Knockdown of 5-HT2AR in mPFC induces compensatory changes in gene networks regulating glutamatergic and GABAergic transmission in mPFC. Thus, a preclinical model of localized mPFC 5-HT2AR deficiency will be useful to explore variations in the functional capacity of the 5-HT2AR.
Financial Support: T32DA07287, P50DA033935

WEDNESDAY, JUNE 15, 2022

POSTER SESSION 4

W1. Alterations in Diurnal Cortisol Related to Cannabis Use Disorder and Recent Marijuana Use: A Pilot in-Field, Within-Person Intensive Monitoring Study

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Previous work suggests that cannabis misuse results in subjective and biological adaptations in stress and motivation, including increases in subjective stress and negative affect, increases in craving, and alterations in cortisol responding to stress and cannabis use. Our recently completed pilot study used a multidomain, intensive data collection approach in the real world to investigate psychological and biological stress adaptations associated with Cannabis Use Disorder (CUD) relative to recreational, non-disordered use (<3x/week).
Methods: Fifteen individuals with CUD (female:55%) and 16 recreational cannabis users (female:53%) were recruited to complete six days of intensive surveys paired with saliva samples. We measured subjective craving, cannabis use, and stress events via eight scheduled smartphone prompts per day for six days. Participants also provided saliva samples in conjunction with six of these eight prompts. Multilevel models were used with person-mean and grand-mean centering to decompose the momentary, within-person fluctuations from between-person differences.
Results: On average, individuals with CUD used more cannabis than light users during the study, $\chi2(1)=17.22$, $p<0.001$. Momentary changes in craving predicted an increased likelihood of cannabis use in the next prompt, $\chi2(1)=7.72$, $p=0.005$. We found evidence of a dampened diurnal cortisol rhythm in individuals with CUD relative to the light users, $F(1,893.8)=4.78$, $p=0.029$. Marijuana use reported in a previous assessment predicted decreased cortisol in the subsequent sample, $F(1,502.3)=4.14$, $p=0.042$. The relationship between recent marijuana use and cortisol was marginally moderated by within-person stress events, $F(1,483.5)=3.68$, $p=0.056$. If a person used marijuana in the previous survey, their cortisol levels increased if there also was a reported stress event during that time.
Conclusions: These findings provide preliminary evidence of alterations in real-world craving and stress responses as a function of cannabis use. Timely interventions that target craving in real time may reduce marijuana misuse and normalize stress responses and stress-related marijuana use in CUD.
Financial Support: KL2 TR001862

W2. Assessing the Utility of the Cannabis Use Disorder Identification Test – Revised (CUDIT-R) in a Sample of Medical and Non-Medical Cannabis Using Veterans

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Few studies have examined the validity of the Cannabis Use Disorder Identification Test – Revised (CUDIT-R) in relation to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5)

criteria for cannabis use disorder (CUD). This study assesses the performance of the CUDIT-R among a sample of veterans with regular cannabis use.
Methods: Primary care patients presenting to one of three Department of Veterans Affairs (VA) medical centers with monthly cannabis use were approached and consented into a longitudinal cohort study. This analysis included individuals of both sexes in the baseline assessment of the cohort study with complete information for all variables used in analyses (n=234). CUDIT-R scores were compared against Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5) CUD as the standard. Measures of validity (sensitivity, specificity, positive predictive value, negative predictive value) were calculated. Optimal CUDIT-R cutoff values were identified using Youden's Index, and receiver operating characteristic (ROC) curves were created to examine diagnostic proficiency of the CUDIT-R. Analyses were also stratified by those with medical and non-medical use, and across DSM-5 severity (general, moderate, and severe CUD).
Results: Among the entire sample, 38.9%, 10.7%, and 3% qualified for AUDADIS-5 general DSM-5 CUD, moderate CUD, and severe CUD, respectively. Optimal CUDIT-R scores for general DSM-5 CUD were identified at 10 (sensitivity: 0.58; specificity: 0.80), at 12 for moderate CUD (sensitivity: 0.72; specificity: 0.82), and 14 for severe CUD (sensitivity: 0.71; specificity: 0.87). ROC curves showed higher CUDIT-R validity among veterans with non-medical versus medical use.
Conclusions: The present study identified optimal CUDIT-R cutoff scores for the veteran cannabis using population. Varying DSM-5 validity measures by medical and non-medical use and severity of cannabis use inform the need for population-specific cutoff values among individuals who use cannabis.
Financial Support: This work was funded by a VA Health Services Research and Development Investigator-Initiated Research Award (IIR 15-348).

W3. Associations Between Maternal Prenatal Cannabis Exposure and Adolescent Cognitive Outcomes From the ABCD Study

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Drug Category Cannabis/Cannabinoids
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Previous studies of prenatal cannabis exposure imply developmental consequences in offspring. However, cognitive outcomes in prenatally exposed adolescents are poorly known. Using data from the Adolescent Brain Cognitive Development (ABCD) Study, we aimed to examine the association between mental rotation outcomes as measured by the Little Man Task (LMT) based on prenatal cannabis exposure before/after knowledge of pregnancy.
Methods: Among 11898 participants ages 9-10 (47.8% female), 9896 met inclusion criteria for analysis. Inclusion criteria included participants whose biological mothers completed questionnaires during their baseline study session querying prenatal cannabis use, and those who also completed the LMT. LMT performance was measured using an efficiency ratio factoring reaction time and percentage of correctly completed trials. Cannabis use before and after knowledge of pregnancy were categorized separately. We conducted a bivariable generalized linear mixed model, nesting participants within families and study sites, to determine an association between prenatal cannabis exposure and efficiency ratio. Then, we conducted a multivariable generalized linear mixed model to control for potentially confounding variables, including participant demographics, maternal socioeconomic demographics, and other prenatal substance exposure.
Results: Bivariable analysis demonstrated an association of prenatal cannabis exposure after knowledge of pregnancy with poorer LMT performance (β = -0.0174, 95% CI = -0.0286 - -0.0062, p = 0.0024). Multivariable analysis found no independent association between performance and prenatal cannabis exposure before/after knowledge of pregnancy (Before knowledge: β = -0.0068, 95% CI = -0.0115 – 0.0034, p = 0.2824; After knowledge: β = -0.0041, 95% CI = -0.0185 – 0.0039, p = 0.1987).
Conclusions: Although we found no significant association between prenatal cannabis exposure and young adolescent mental rotation, brain activity analysis during mental rotation tasks is needed to further compare groups. Pregnant women should still exercise caution regarding cannabis use considering previously established fetal outcomes from prenatal exposure.

Financial Support: supported by NIDA DA047296

W4. Effect of COVID-19 on Cannabis Use and Motivation to Quit Among a Community Sample of Cannabis Users: A Time Series Analysis

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The objective is to examine an association between cannabis use and motivation to reduce cannabis and COVID-19 lockdowns over time.
Methods: An interrupted time series analysis was conducted using screening data from a prospective cohort study on cannabis use effects on functional domains. Screening by trained interviewers collected participant's age, California residency status, treatment status, cannabis use frequency, hazardous alcohol use, access to technology and motivation to reduce cannabis use, derived from the Marijuana Problems Scale. The pre-COVID period was defined as November 1, 2019-March 14, 2020. COVID-19 benchmarks included three California lockdowns in 2020. A statewide shelter in place order (March 19, 2020) and business closure orders amid a summer (July 13, 2020) and a winter surge (November 15-19, 2020). Using segmented regressions, we estimated step changes and trend changes after each lockdown. Data were collapsed into weekly means, including mean weekly age, proportion of respondents in treatment for cannabis use, mean cannabis use frequency (days/week), and days since last use.
Results: Trend in motivation to reduce increased after the third lockdown after adjusting for age of respondents, quarter of the year, and proportion of respondents in cannabis use treatment (point estimate: 0.17, 95%CI: [0.07, 0.27]). The first lockdown was also associated with an increase in cannabis use frequency in comparison to the pre-COVID period, though this did not meet statistical significance (point estimate: 0.46 days/week, 95% CI: [-0.01, 0.93]. Otherwise, we found no appreciable changes in cannabis use over the pandemic.
Conclusions: As respondents prepared to return to work and experienced lesser social restrictions, motivations to reduce use increased though cannabis use remained unchanged. This study adds to the literature on the impact of the COVID-19 pandemic on cannabis use.
Financial Support: National Institute on Drug Abuse (DA042280)

W5. Exploring the Role of Female Gender Discrimination on Problematic Cannabis Use With Race as Moderator

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Drug Category Cannabis/Cannabinoids
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Previous research has found that gender discrimination is associated with increases in stress and externalizing behaviors amongst disadvantaged female populations. The current study examined the effect of gender discrimination on problem cannabis use within a racially and ethnically diverse sample of females. The study also examined whether race or ethnicity moderated the association between gender discrimination and problem cannabis use.
Methods: Three hundred female participants between the ages of 18 and 35 (M = 22.24; SD = 5.25) completed an online questionnaire that included self-report measures on experiences with gender discrimination and past-year problem cannabis use. A linear regression was performed to test the association between gender discrimination and cannabis use, and the moderating effect of race and ethnicity.
Results: Results indicated a direct effect between gender discrimination and problem cannabis use [F (1, 312) = 11.142, p < .001]. Race also had a significant moderating effect. Specifically, there was a significant conditional effect for Black women [t (286) = 3.766, p < .001] with a non-significant effect for White women [t (286) = -.3440, p =.7311]. A marginally significant effect was found for Asian [t (286) = 1.952, p

< .0519] and Native American women [t (286) 1.895, p <.0591] with a non-significant effect for White women. Finally, a significant conditional effect was found for non-Hispanic women [t (311) = 3.719, p < .001] with a non-significant effect for Hispanic women [t (311) = .3914, p =.6598].
Conclusions: The findings from the study stress the importance of understanding the effect that gender discrimination can have on cannabis use among women, and variation in risk based on race and ethnicity. Such findings can inform the implementation of intervention programs for at risk female adults to reduce problem cannabis use and related health outcomes.

W6. Gender Differences in Cannabis Use Disorder Symptoms: A Network Analysis

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Drug Category Cannabis/Cannabinoids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: While cannabis use in women is increasing worldwide, research into gender differences in cannabis use disorder (CUD) symptomology is lacking. In response to limited effectiveness of addiction treatment, research focus has been shifting from clinical diagnoses towards interactions between symptoms as patterns of symptoms and their interactions could be crucial in understanding addictive processes. The aim of the current study was to evaluate the CUD symptom network and assess whether there are gender differences therein.
Methods: A total of 1257 weekly cannabis users, including 745 men and 512 women participated in the study. All participants completed online questionnaires assessing the MINI DSM-5 CUD symptoms and additional items on cigarette use and the presence of psychological diagnoses. Gender differences were assessed for all variables and the Ising model was used to estimate the networks in men and women, applying network comparison tests to assess differences.
Results: The estimated networks were dense with all symptoms except 'Tolerance' and 'Risky Use' being highly central. There were gender differences in the prevalence of 6 of the 11 symptoms, but symptom networks were similar between men and women. Cigarette use appeared to be primarily connected to the network through withdrawal, indicating a potential role of nicotine use in cannabis withdrawal. Furthermore, there were gender differences in the associations of mood and anxiety disorders with the network, indicating potential gender differences in how comorbidities are associated with CUD symptoms.
Conclusions: While men and women differ in symptom prevalence, the pattern and strength of the interactions between symptoms appear similar. However, the relation between cigarette co-use and withdrawal, as well as gender differences in the role of anxiety and mood disorders in the CUD network highlight the importance of research into comorbidity and gender difference therein and how this could affect treatment outcomes.
Financial Support: This research was supported by grant 1R01 DA042490-01A1 awarded to Janna Cousijn and Francesca Filbey from the National Institute on Drug Abuse/National Institute of Health.
First and second authors contributed equally to the research.

W7. Open Board

W8. Patterns of Tobacco and Cannabis Use in Australia: A Latent Class Analysis and Health-Related Correlates

Carmen Lim*[1], Janni Leung[1], Shannon Gravely[2], Coral Gartner[3], Vivian Chiu[1], Tianze Sun[1], Jack Chung[1], Daniel Stjepanović[1], Jason Connor[1], Roman Scheurer[4], Wayne Hall[1], Gary Chan[1]
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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research

Aim: Tobacco and cannabis are the most commonly used substances after alcohol in Australia. This study examined the patterns of tobacco and cannabis use and their associations with socio-demographic, health-rated correlates and past-year alcohol and illicit substance use.
Methods: Data are from the 2019 Australia National Drug Strategy and Household Survey (n=22,015). Latent class analysis was used to identify groups of respondents that are similar based on their tobacco and cannabis use patterns. The socio-demographic, health-rated correlates and past-year substance use of each latent class was examined using multinomial logistic regression. Analysis were weighted to adjust for differential probabilities of selection within households and non-response.
Results: A four-class solution was identified: co-use of tobacco and cannabis (2.4%), cannabis only (5.5%), tobacco only (8.0%), and non-user (84.0%). Compared to the non-user class, all other classes were likely to be: male, younger (18-29 years), experiencing high levels of psychological distress, using illicit substances in the last year, and report heavy alcohol consumption. The odds of being in the co-use class was higher for those reported past-year illicit substance use and high-risk alcohol consumption compared to those in the single substance classes. Within the co-use class, 78.4% had mixed tobacco and cannabis while 89.4% used alcohol with cannabis on at least one occasion.
Conclusions: Many respondents were using either tobacco, cannabis, or both substances. Mental health issues and the poly-substance use across all substance use classes is concerning, in particular the co-use class. Existing policies need to minimize further harms related to tobacco and cannabis to reduce societal burden associated with both substances.
Financial Support: National Health Medical Research Council (NHMRC) of Australia Postgraduate Scholarship [APP2005317]; The University of Queensland Living Stipend and Tuition Scholarship, National Centre for Youth Substance Use Research (NCYSUR) PhD top-up scholarship

W9. Social Network Analysis of Young Adults' Cannabis Use Before and During the COVID-19 Pandemic

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: The COVID-19 pandemic, which has caused historic morbidity and mortality, has also disrupted young adults' social relationships. Little is known about the extent to which young adults changed the number of people who they used cannabis with, or what factors were associated with changes before and during the pandemic.
Methods: 108 young adult cannabis users in Los Angeles (40.2% medical cannabis patients) reported on their egocentric social network characteristics, personal cannabis use, and pandemic-related variables before and during the COVID-19 pandemic. Multinomial logistic regression identified factors associated with increasing or maintaining (vs. decreasing) the number of people (alters) young adults used cannabis with before and during the pandemic. Multilevel modeling identified ego (participant) and alter-level factors associated with dyadic cannabis use during the pandemic (at follow-up).
Results: Most egos (n=66; 61%) decreased the number of alters they used cannabis with, 15 (14%) maintained, and 27 (25%) increased. Having fewer cannabis-using alters who provided social support (RRR=0.52, p=0.03) and greater time known one's alters (RRR=8.47, p=0.001) were associated with maintaining (vs. decreasing); larger egonetwork size (RRR=0.67, p=0.03) and living with family during the pandemic (RRR=0.21, p=0.045) were associated with decreasing (vs. increasing); greater time known one's alters (RRR=6.60, p<0.001) was associated with increasing (vs. decreasing). During the pandemic, egos were more likely to use cannabis with alters who also used alcohol with the ego (OR=24.64, 95% CI: 8.11, 74.89), and alters with more positive attitudes towards cannabis (OR=9.30, 95% CI: 5.16, 16.78).
Conclusions: Results identified significant factors illustrating how cannabis-using young adults navigated their cannabis use during a time of great uncertainty and varying levels of social-distancing, and further inform our understanding of COVID's impact on young adults' cannabis use.
Financial Support: This research was supported by NIDA grants R01DA034067 and F31DA053779

W10. The Association Between Workplace Drug Use Policies and Current Drug Use Among Low-Income Workers: Findings From the National Survey on Drug Use and Health

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Poverty and drug use are inextricably and bidirectionally related, but the workplace may represent an opportunity for intervention among low-income workers. Although many employers have policies regarding substance use, they vary with respect to punitiveness and resources made available to employees, which may have differential effects on employee drug use.
Methods: Using cross-sectional data from the 2019 National Survey on Drug Use and Health, we used separate regression models to examine the associations between several organizational-level workplace factors and current drug use (i.e., cannabis use, criminalized drug use, and misuse of prescription psychotherapeutic drugs) among workers aged 18-64 years living at or below 200% the federal poverty level (N = 7,953). Final models controlled for age, sex, race-ethnicity, and work status (full-time vs. part-time).
Results: Having any written policy on employee substance use was associated with a lower odds of current cannabis use ($p < 0.001$), criminalized drug use ($p < 0.001$), and misuse of prescription psychotherapeutic drugs ($p < 0.01$). Workers who reported receiving educational information on substance use at their workplace were less likely to report current cannabis use ($p < 0.01$) and use of criminalized drugs ($p < 0.05$). Likewise, having an employee assistance program (EAP) to address problems with drug use was associated with a lower odds of current cannabis use ($p < 0.001$) and criminalized drug use ($p < 0.01$). However, testing employees for drug use during the hiring process ($ps > 0.05$) and having a policy in place to terminate current employees who test positive for drugs ($ps > 0.05$) were not associated with drug use.
Conclusions: Results suggest that providing employee-centric resources related to drug use (i.e., education, EAP) may be more effective than punitive policies (i.e., pre-employment drug testing, termination for drug use) in preventing drug use among low-income workers.

W11. The Association Between Cannabis Use Disorder and Co-Occurring Anxiety and Depression

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Drug Category Cannabis/Cannabinoids
Topic Comorbidities
Abstract Detail Human
Abstract Category Original Research
Aim: Anxiety and depression are associated with cannabis-related problems. Emerging literature finds that reductions in cannabis use may be associated with improvements in anxiety or depression over 12-week period. The objective of the current study is to extend this research by examining the relationship between long-term reductions (i.e., up to 6 months) in cannabis use and depression, generalized or social anxiety among a community sample of individuals with cannabis use disorder (CUD).
Methods: This study recruited 152 participants with CUD. Assessments at baseline, 3- and 6-month follow up included past month substance use as well as the Hospital Anxiety and Depression Scale to measure generalized anxiety, the Social Interaction Anxiety Scale to measure social distress and the Patient Health Questionniare-8 to measure current depression. Baseline surveys also captured demographics and assessments also included treatment history and current cannabis use disorder. Based on the trajectory of cannabis use for each individual up to the 6-month follow up, individuals were classified into the reduced cannabis use group (n=52) and non-reduced cannabis group (n=100). T-tests and chi-square tests did not reveal any demographic differences between the reduction and non-reduction groups except for age. We then examined the associations between cannabis use and psychiatric outcomes over time by mixed effect models, which included covariates of age, gender, race/ethnicity, and treatment history

Results: We find that increasing days of cannabis use per week is positively associated with higher scores of depression and social anxiety, but not generalized anxiety, among people of similar age, gender, education, race, and treatment history.
Conclusions: This work adds to the emerging literature on CUD and co-occurring depression and social anxiety. Further research may identify outcomes that demonstrate clinically meaningful improvement in association with reduced cannabis use among long-term users and may facilitate improvement in treatment intervention efforts for CUD.
Financial Support: This study was funded by National Institute on Drug Abuse (DA042280)

W12. The Lateral Habenula: A Critical Crossroad for the Brain's Negative and Positive Valence Systems

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Drug Category Cannabis/Cannabinoids
Topic Imaging
Abstract Detail Human
Abstract Category Original Research
Aim: The interaction between negative and positive valence systems is critical in terms of prevention and intervention strategies in substance use disorders (SUDs). Here, we tested a model that lateral habenula (LHb) signaling may be important in reward prediction error (RPE) – or the "psychological distress" following mismatched expectations that modulates response to rewards. We hypothesized that (1) reward prediction error will modulate the functional connection in the LHb and (2) increased functional connectivity between the LHb will be associated with greater negative mood symptoms and greater reward seeking behavior.
Methods: Ninety-eight participants (56 males) received an fMRI scan while performing the Monetary Incentive Delay (MID) task to measure incentive motivation to monetary gains and losses. Psychophysiological interaction analysis (PPI) was performed with the lateral habenula as seed region to determine LHb functional connectivity during RPE defined as reward wins > reward losses. A regression analysis was conducted to test the relationship between LHb functional connectivity and substance use behaviors via IMPSS.
Results: Greater functional connectivity between LHb and orbitofrontal cortex (OFC) was found during RPE ($p < 0.05$, $Z \geq 2.3$). Greater LHb-OFC connectivity was associated with greater IMPSS scores.
Conclusions: Our findings suggest that the LHb is an important hub for moderating the interaction between valence systems during RPE. Characterizing these underlying mechanisms can advance our understanding of how dysfunction in the LHb may have wide-ranging downstream consequences for SUDs.
Financial Support: This research was funded by a National Institute on Drug Abuse/National Institutes of Health grant: #KO1 DA021632 to Francesca Filbey.

W13. Age Differences in Patterns of Cannabis and Other Drug Use Within a Cohort of Medical Cannabis Patients in Pennsylvania

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: A medical cannabis program was launched in Pennsylvania in 2016. However, no study has reported on past and current patterns of cannabis and other drug use with a population of Pennsylvania medical cannabis patients (MCPs).
Methods: MCPs (n=112) aged 20-71 years (45.5% male) were surveyed about histories and current practices of cannabis and other drug use between June-November 2021. Bivariate analysis examined potential differences in cannabis and other drug use histories/practices between younger (20-30 years old) and older (31 year and older) adult MCPs using Chi-Square and Kruskal Wallis tests.
Results: Younger MCPs reported earlier age of regular/daily and medicinal cannabis use initiation ($p<0.01$). Greater proportion of younger MCPs reported using cannabis concentrates ($p<0.05$). Both younger and older

MCPs used cannabis at similar frequency (past-90-day mean= 82.5 days) and amount (43.9% used up to 7 grams per week). No significant differences were observed for lifetime and past-90-day other drug use. However, younger MCPs were trending towards lower lifetime stimulant/opioid use (i.e., methamphetamine, crack, heroin) but higher past-90-day alcohol, hallucinogens and sedatives/hypnotics use.
Conclusions: Our findings highlight earlier in life exposure to cannabis among younger MCPs while cannabis use frequency and amount consumed were similar between younger and older MCPs. Lifetime and past-90-day trends of use of other substances might indicate maturing out of drug use among older MCPs and experimentation phase among younger MCPs. Further monitoring of cannabis and other drug use trends is warranted.
Financial Support: Agronomed Biologics

W14. An Exploration of Multivariate Symptom Clusters of Cannabis Use Disorder in Young Adults

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Cannabis use disorder (CUD) is prevalent in young adults and is commonly comorbid with additional mental health difficulties. Since the release of the DSM-V, CUD is understood as a unidimensional construct. However, continued research has identified several symptom clusters within substance use disorder criteria that may pose separate risk factors and functional difficulties. The current study aims to examine how symptom clusters commonly manifest in young adults that use cannabis using a latent class approach and explore how these clusters are related to commonly co-occurring mental health difficulties.
Methods: Participants were recruited for a study on externalizing psychopathology. 1,174 young adults, aged 18-34, participated in a series of in-person assessments. Using items from the Semi-Structured Interview on the Genetics of Alcoholism (SSAGA), Latent class analysis (LCA) was conducted on 17 criteria that align with DSM-V CUD. To examine associations between class membership and commonly co-occurring psychopathology, identified latent classes were characterized using multinomial regressions to predict mental health symptoms.
Results: LCA results identified a "No problems" class (2% of sample), a "Low problems" class (25% of sample) characterized by moderate probability of endorsing consumption items, a "Moderate without withdrawal" class (9% or sample) characterized by endorsing consumption and loss of control items but minimal endorsement of withdrawal items, a Moderate with withdrawal" class (7% of sample) characterized by moderate probability of endorsing all item types, and "Severe" class (5% of sample) characterized by high probability of endorsing all items. Multinomial regression analyses generally indicated global mental health difficulties increased with class membership.
Conclusions: While results appear consistent with a increasing problems being associated with increasing symptom endorsement, there are some qualitative differences in symptom endorsement, especially for those in our sample with moderate/severe problems. Findings suggest intervention efforts may benefit from treatment targeted at various presentations of CUD presentation.
Financial Support: This research was supported by National Institutes of Alcohol Abuse and Alcoholism grant [R01AA13650] to Peter Finn, National Institutes of Drug Abuse (NIDA) grant [T32 DA24628] to Lindy Howe, National Institutes of Mental Health grant [T32 MH103213] to Allen Bailey, and National Institutes of Alcohol Abuse and Alcoholism [T32 AA07462] grant to Polly Ingram.

W15. Cannabis Practices of Gender Minority and Cisgender Young Adults Recruited Through Social Media

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Drug Category Cannabis/Cannabinoids

Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Men have reported greater cannabis consumption than women. While less is known about gender minorities [GM; transgender, non-binary], a recent review revealed higher rates of use compared to cisgender counterparts. The present study compared cannabis use practices in young adults of diverse gender identities: GM, cisgender men [CM], and cisgender women [CW].
Methods: Participants aged 18–34 (N=2402) were drawn from a Facebook/Instagram recruited sample of adult cannabis users (recruited May–July 2021). Online survey items assessed sociodemographic characteristics and past week method, potency, frequency (total days and times of day), and quantity of cannabis use in number of hits/puffs/tokes per day, grams per week, or joints per week. Median splits coded frequency and quantity (high vs. low) of use, which were combined to create a four-group "frequency/quantity" variable. Chi-square and ANOVA analyses explored gender differences. Two multinomial logistic regressions predicted "frequency/quantity" category of plant and concentrate use based on gender identity.
Results: GM and CW reported using lower potency products than CM (p's<.05). GM reported fewer mean days of use in the past week than CW (p=.02) and were more likely to report using cannabis only during the evening and night times of day (24.0%) compared to CM (16.9%) and CW (16.4%). Compared to CM, GM reported lower quantity of flower (in grams) consumed over the past week. Regression models revealed lower odds of high frequency/high quantity flower (p=.015) and concentrate (p=.005) use among GM relative to CM.
Conclusions: Within this sample of young adult cannabis users, findings suggest that those identifying as GM reported lower frequency of cannabis use compared to CM and CW. GM reported lower quantity of cannabis use compared to CM. Future work should replicate and expand upon initial findings to explore gender differences in cannabis use patterns and associated problems.
Financial Support: R01DA050032; P30DA029926; T32DA037202

W16. Chronic Relief: Exploring the Use and Impact of Cannabis in the Setting of Chronic Pain Among Black American Pain Patients in Los Angeles

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Drug Category Cannabis/Cannabinoids
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: AIM 1: To document the subjective experience of chronic pain, its management using traditional analgesics +/- cannabis, and social/cultural experiences faced by Black female and male Americans who are occasional (i.e., once per week) and frequent (i.e., daily) cannabis users aged 18-60 in Los Angeles.
Methods: Subjects (n=21) completed a self-administered drug screening, quantitative baseline survey, and semi-structured qualitative interview. Data were collected on patients' experience with chronic pain, history of depression and anxiety, cannabis use, impulsivity, impulse inhibition, and risk for drug dependence.
Results: Preliminary results from our qualitative interviews show three main findings on cannabis' analgesic effects, mode of administration, and unique racial experiences of using cannabis while Black. All participants found cannabis to significantly reduce pain ratings. However, over 75% of participants co-used cannabis and tobacco. Additionally, our results should reveal some of the environmental and sociological factors that have influenced Black Americans to use cannabis for pain management. These factors may include but are not limited to physician mistrust, healthcare discrimination, distrust of pharmaceutical companies, and preference for alternative medicines. Finally, over 50% of respondents cited experiencing discrimination at retail locations (e.g., dispensaries) while using purchasing cannabis and a small number of respondents reported criminal justice issues/police incidents as it related to their legal cannabis use.
Conclusions: We find that cannabis has significantly and positively impacted the pain ratings of Black Americans in Los Angeles. Despite the therapeutic benefits of pain relief, a troubling trend emerged in cannabis and tobacco co-use. Cannabis and tobacco co-use produce additive and/or synergistic adverse health impacts including greater exposure to toxins and carcinogens as well as increased risk for cannabis

use disorder. Black Americans also experience unique racial and sociological factors relating to their use (e.g. "using cannabis while Black") which may be different from how their white counterparts may experience use.
Financial Support: R25NS094093

W17. Community Reinforcement and Family Training for Early Psychosis (CRAFT-EP) and Substance Use in Reducing Family Members' Distress: Preliminary Assessment of Efficacy

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Drug Category Cannabis/Cannabinoids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use is associated with poor treatment outcomes in early psychosis, and often remains a challenge for clients and families. Families of individuals with psychosis and substance use can assist their loved ones by improving client-family interactions and providing a supportive environment conducive to change. Community Reinforcement and Family Training adapted for early psychosis (CRAFT-EP) works with family members to encourage substance use change, decrease families' distress and improve client-family relationships. This poster presents preliminary descriptive results of efficacy measures regarding family distress and relationship quality.
Methods: Participants were male and female family members (N=20) of a relative with early psychosis and a history of cannabis, alcohol, or nicotine use. Participants completed six to eight telehealth coaching sessions in an open clinical trial. We present pre-post intervention changes in the current poster. Measures of family member distress and relationship quality include the Beck Depression Inventory (BDI-II), the State-Trait Anxiety Inventory-Short Form (STAI-SF), the Perceived Stress Scale (PSS), the Happiness Scale, and the Relationship Happiness Scale. We calculated the estimated mean change from pre-intervention with 95% confidence intervals (CI) and standardized effect sizes (Cohen's d).
Results: Family members had substantial reductions in depression on the BDI-II (estimated mean change -5.85 [95% CI -8.9, -2.7]; d=0.87) and perceived stress on the PSS (-4.0 [-7.3, -0.6]; d=0.6). Participants demonstrated smaller decreases in anxiety on the STAI-SF (-1.1 [-2.2, -0.0]; d=0.5), increases in relationship happiness on the Relationship Happiness Scale (8.4 [0.1, 16.8]; d=0.5), and personal happiness on the Happiness Scale (3.4 [-0.8, -7.5]; d=0.4).
Conclusions: Results of these preliminary analyses suggest that CRAFT adapted for early psychosis may be helpful at reducing family members' distress, particularly in terms of depression and perceived stress, and increasing relationship satisfaction.
Financial Support: NIDA 1K23 DA050808-01

W18. Empirically Derived Patterns of Motivation, Readiness, and Confidence to Stop or Reduce Cannabis Use Among Treatment-Interested Adolescents and Emerging Adults

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Drug Category Cannabis/Cannabinoids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Among individuals interested in treatment for cannabis use, motivation, readiness, and confidence in their ability to quit or reduce is variable. The primary objective of the current study was to determine how levels of motivation, readiness, and confidence, measured on 11-point scales from 0 to 10, interact and form empirically derived profiles in a sample of treatment-interested adolescent and emerging adult cannabis users (N= 120, 51.7% female; 77.5% white; 13.3% Hispanic/Latino; Mage = 19.1).
Methods: A Latent Profile Analysis was conducted in which we tested four latent profile models of 2-,3-,4-, and 5-class solutions.

Results: Empirically validated predefined factors were used to compare the models, and a four-class solution was selected: Low (n= 19, 15.8%), Ambivalent (n= 30, 25%), Ambivalent Confident (n= 25, 20.8%), and High (n= 46, 38.3%). Low and High groups were characterized by low or high motivation (Low Est. = 3.07, SE = 0.30; High Est. = 7.91, SE = 0.31), readiness (Low Est. = 2.53, SE = 0.43; High Est. = 8.15, SE = 0.23), and confidence (Low Est. = 3.38, SE = 0.46; High Est. = 8.40, SE = 0.27), respectively. The Ambivalent group was characterized by mid-range scores across all three indicators (Motivation Est = 5.78, SE = 0.38; Readiness Est. = 5.07, SE = 0.27; Confidence Est. = 4.60, SE = 0.35). Ambivalent Confident group members tended to report mid-range motivation (Est. = 4.66, SE = 0.28) and readiness (Est. = 4.36, SE = 0.49) but high confidence (Est. = 9.00, SE = 0.23) in their ability to quit or reduce their cannabis use.
Conclusions: Our results demonstrate that there are distinctive groups within adolescents and emerging adults interested in addressing their cannabis use. Clinically, these profiles may be used to facilitate the process of intervention selection and approach.
Financial Support: T32DA007288 (Postdoctoral Fellow: Gex); R01DA042114 (PI: Gray)

W19. Exploring Trajectories of Days of Cannabis Use Among Young Adults: A Novel Mixed Methods Study

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Drug Category Cannabis/Cannabinoids
Topic Lifespan (Infant, Adolescent, Aging)
Abstract Detail Human
Abstract Category Original Research
Aim: Few studies have examined trajectories of days of cannabis and other drug use among young adult cannabis users before and after legalizing cannabis for personal use in California in 2016.
Methods: A longitudinal study of young adult medical cannabis patients and non-patient users in Los Angeles (aged 18-26 in 2014) were interviewed quantitatively (annually/quarterly) and qualitatively (annually) between 2014 and 2021. Adopting a novel explanatory mixed-methods approach, participants reported 90-day cannabis and other drug use over a 7-year study period via quantitative surveys. During subsequent qualitative interviews in 2021, a select group of 18 participants were presented graphs depicting patterns of their 90-day cannabis and other drug use across the study period and asked to qualitatively describe individual and policy-level factors influencing changes in drug use.
Results: Most participants consumed high levels of cannabis in 2014, e.g., 70-90 days out of 90, and then reported by 2021 either: maintaining high levels of use with occasional dips or declining use ranging from moderate, e.g., 20-50 days, to steep, e.g., 0-20 days. While increasing trajectories of days of cannabis use between 2014-21 were rare, many reported periodic increases following decreases. Increases in days of cannabis use were attributed to: changes in settings/relationships where cannabis use was normative; drug substitution, e.g., cannabis for alcohol; and disruptions linked to COVID-19. Decreases in days of cannabis use were attributed to: changes in settings/relationships where cannabis was scarce/infrequently used; job-related factors; health concerns, e.g., pregnancy; and high costs of cannabis. Most other drug use, e.g., alcohol, nicotine, or illicit, declined or were reported at very low levels across the 7-year study period.
Conclusions: While personal milestone events and health were often reported by young adults as factors explaining increases or decreases in cannabis and other drug use, broader policy-related events, e.g., legalizing cannabis, storefront sales, were rarely described.
Financial Support: NIDA – R01DA034067-01A1

W20. Longitudinal Examination of Obsessive Passion for Cannabis Use Among College Undergraduate Students

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder

Abstract Detail Human
Abstract Category Original Research
Aim: Obsessive passion refers to a relationship with an activity that has become so compelling that it causes conflicts with other activities and one's values. This study aims to evaluate whether obsessive passion for cannabis use is associated with future cannabis use, use-related consequences, and cannabis use disorder (CUD) symptoms among college undergraduates who reported recent cannabis use.
Methods: Data include baseline (11/2020) and five-month (5m; 05/2021) follow-up from a longitudinal prospective cohort study of undergraduates at a large public university in the mid-Western United States (N=241; Mean age=20.63, SD=2.56; proportion with 2+ CUD symptoms=56%; female=56.0%; White=88.4%; heterosexual/straight=68.9%). Descriptive analyses, correlations, and paired samples t-tests were conducted.
Results: First, higher baseline obsession passion for cannabis use was significantly correlated with more days of cannabis use (r=.49; p<.001), cannabis use-related consequences (r=.54; p<.001), and CUD symptoms (r=.64, p<.001) at 5m follow-up. Second, compared to cannabis use at baseline, participants reported an increase in obsession passion for cannabis use at follow-up (p<.001; d=.28). Third, comparing baseline obsessive passion scores against other potential factors related to future cannabis use, obsessive passion was more strongly related to cannabis use at follow-up compared to baseline number of CUD symptoms (r=.35; p<.001) and number of use-related consequences (r=.24; p<.001). Interestingly, baseline levels of depression, anxiety, emotion regulation, psychological flexibility, and motivation to change were unrelated to cannabis use at 5m (ps>.05).
Conclusions: Baseline obsessive passion for cannabis use was associated with greater cannabis use, CUD symptoms, and cannabis use-related consequences at 5m follow-up and was more strongly related to future cannabis use than CUD symptoms or use-related consequences. Findings suggest that obsessive passion could be of utility in understanding cannabis use behaviors in this at-risk population. Future studies are needed to explore whether intervening on obsessive passion could reduce future cannabis use or related consequences.
Financial Support: Funding for this study came from a competitive seed grant from the College of Social Work at Ohio State University. AKD, is supported by private philanthropic funding from Tim Ferriss, Matt Mullenweg, Craig Nerenberg, Blake Mycoskie, and the Steven and Alexandra Cohen Foundation. AKD, SA, and YX are supported by the Center for Psychedelic Drug Research and Education, funded by anonymous private donors. The funding sources had no role in the study, data analysis, interpretation, or communication of findings.

W21. Pharmacokinetic and Pharmacodynamic Effects of Hemp-Derived Topical Cannabidiol (CBD) Products

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: Topically-applied cannabidiol (CBD) products have proliferated since hemp (cannabis containing <0.3% THC) was legalized but clinical studies on these products are lacking. This study characterized the pharmacokinetic (PK) and pharmacodynamic (PD) effects of various commercially-available CBD-dominant topical hemp products.
Methods: Eleven infrequent cannabis/CBD users were randomized to use either a CBD-dominant cream (N=8; CBD dose=11mg; THC dose=0.7mg per application), a placebo cream (N=2), or a CBD-dominant lotion (N=1; CBD dose=95mg; THC dose=4.2mg). Participants completed an 8-hr drug application session in the laboratory, followed by a 10-day outpatient drug application period (b.i.d. dosing); participants returned to the lab on Days 2, 3, 7, 10, and 17 (1-week washout). Blood, urine, and oral fluid (OF) were collected and PD effects were assessed during the laboratory session and the outpatient visits.
Results: Subjective/cognitive effects and vitals were similar at baseline and all post-dosing timepoints. Trace concentrations of THC were detected in OF for all CBD-dominant cream participants but THC

concentrations never exceeded 4ng/mL (threshold for a "positive" cannabis test). The participant who used the CBD-dominant lotion had several OF samples with THC concentrations >4ng/mL. All urine specimens for 5 CBD-dominant cream participants were negative (screening cutoffs: 20, 50, 100ng/mL). Remaining urine and blood samples are pending analysis. Overall, among active product participants, OF CBD concentrations increased steadily throughout the study, peaked during the outpatient phase, and decreased markedly at the washout visit.
Conclusions: The topical CBD products examined did not produce significant PD effects. The CBD-dominant cream did not produce positive results on urine or OF drug tests for cannabis/THC, but positive OF results were observed in the first CBD-dominant lotion participant. The observed increases in OF cannabinoid concentrations (particularly CBD) is suggestive of transdermal absorption. More research is needed to explore how factors such as formulation and dose impact PK/PD effects of topical cannabinoid products.
Financial Support: Substance Abuse and Mental Health Services Administration (SAMHSA) and The Department of Defense (DoD)

W22. The Effects of Stress and Cues on Craving for Cannabis

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Stress has been linked to greater risk of using cannabis. Exposure to cannabis-related cues has been shown to increase cannabis craving, although links between cue exposure and craving to subsequent cannabis use are less clear. We used a hybrid drug-cue exposure and choice procedure to examine links among cannabis-cue exposure, craving, and seeking, and whether pharmacologically-induced stress affects these links.
Methods: Eleven (5M) healthy adults (37.5 ± 10 yrs) with moderate Cannabis Use Disorder (CUD) were housed on an inpatient unit throughout testing. In 6 sessions (Stress X Cue within-subject, placebo-controlled, randomized crossover) they were pretreated with yohimbine (0 vs 20 vs 40 mg oral), an α_2 2-adrenoceptor antagonist that produces anxiety-like effects, exposed to cues (neutral vs cannabis), and worked on a progressive ratio choice task to earn up to 11 puffs from placebo (0.0% THC, with $2/choice) vs cannabis (6.0% THC, without money) cigarettes. Self-administration of their choice then followed. Craving was assessed using VAS items "I feel…" "an urge for marijuana," "a desire to use marijuana," and "a craving for marijuana."
Results: Repeated measures analysis of covariance (ANCOVA) was conducted on peak craving scores in each condition, using session baseline craving levels as covariates. Results for each VAS item were nearly identical so only "Urge for marijuana" is reported. Main effects for yohimbine dose ($F(2,8)=9.25$, $p=.011$, partial $\eta 2=.73$) and cue type ($F(1,8)=6.33$, $p=.036$, partial $\eta 2=.442$) indicate that individuals reported increased "Urge for marijuana" after 40 mg relative to 20 mg yohimbine, and after cannabis compared to neutral cue exposure. Neither cue exposure nor induced stress altered cannabis choice.
Conclusions: Findings indicate that a higher level of pharmacologically induced stress was associated with increased cannabis craving, regardless of cue exposure, but did not increase cannabis seeking. Similarly, cannabis cue exposure elevated craving but did not increase cannabis seeking in this population.
Financial Support: NIH R21 DA040150 (LHL), Gertrude Levin Endowed Chair in Addiction and Pain Biology (MKG), Michigan Department of Health and Human Services (Lycaki/Young Funds)

W23. Use of Pain Medication and Cannabis by Age Groups Before and After Legalization of Cannabis: An Investigation of Trends From 2017 to 2019 in a Representative Sample of Canada

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human

Abstract Category Original Research
Aim: Recent reports of increasing prevalence of self-reported pain in the population and concerns with opioid use/misuse have led to testing of alternative pain medicines, including cannabinoids. The legalization of cannabis in Canada (2018) has presented an opportunity to study potential changes in patterns of prescription opioid and cannabis use on a broad scale. This study investigated differences in prescription opioid and cannabis users stratified by age groups between 2017 to 2019.
Methods: Data were retrieved from the 2017 and 2019 Canadian Alcohol, and Drugs Survey, conducted employing two-phase stratified random sampling of households. Present analyses included respondents ≥25 years old reporting ever using prescription opioid medication, stratified by age (25-44, 45-64, 65+ years).
Results: 2,925 adults (58% female) from 2017 and 4,530 (58% female) from 2019 reporting any lifetime prescription opioid use were identified for analyses. From 2017 to 2019, there was an increase in proportion of individuals aged 45-64 reporting past 12-month prescription opioid use ($X2=18.2$, $p<.001$) and increases across all age groups for past 12-month cannabis use (X2 ranged 6.0-45.9, all p's<.05). Across recent cannabis users of all ages, there was an increase in individuals reporting cannabis use for medical reasons (X2 ranged 77.6-283.9, all p's<.001). Of these medical cannabis users, there was decrease in problematic cannabis use risk from 2017 to 2018 (Fs ranged 22.8-190.9, all p's<.001).
Conclusions: This study reports an overall increase in opioid and cannabis use across age groups in lifetime prescription opioid users following the legalization of cannabis. Findings are congruent with recent USA reports of increasing prevalence of pain problems across ages ≥25 years old. Given the cross-sectional design of this study, the etiology of observed changes in opioid and cannabis use patterns cannot be determined. Thus, future longitudinal investigations are needed, such as in regions where cannabis legalization is being considered.
Financial Support: Initial study sponsors: Health Canada
Sponsors for secondary analyses: Canadian Centre for Substance Use and Addiction

W24. Anxiety in a Placebo-Controlled Pharmacotherapy Trial for Adolescent Cannabis Use Disorder

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Cannabis use disorder (CUD) and anxiety often co-occur in adolescents, and more work is needed to parse the relationship between anxiety and CUD treatment-associated changes in use patterns. This study aims to assess how cessation of or reduction in cannabis use is associated with changes in anxiety severity, particularly among those with higher baseline anxiety.
Methods: Secondary analysis, performed in the context of a randomized controlled trial of pharmacotherapy for CUD, assessed the relationship between self-report anxiety and urine cannabinoid tests (UCT) among 84 adolescent participants over 8 weeks of treatment and follow up. Linear mixed effects models were utilized to determine the association of anxiety and UCT. Revised Child Manifest Anxiety 2nd edition (RCMAS-2) scales were obtained throughout the study, with a raw score greater than 15 indicating clinically significant anxiety. UCT included both quantitative creatinine corrected cannabinoid levels and qualitative results (cutoff for negative <50 ng/ml).
Results: There was no statistically significant association between RCMAS-2 scores and concurrent UCT. Among participants with high baseline anxiety, cessation (indicated by a negative UCT) was associated with a greater numerical reduction in anxiety ($\Delta=-3.5$ (SE=1.7), $p=0.058$) with similar trend-level association between RCMAS and cannabinoid levels at the end of treatment ($\beta=2.32$ (SE=0.55), $p=0.055$). However, associations at earlier time points in the study as well as follow-up were not consistent and associations in those with low/no baseline anxiety were not clinically or statistically significant.
Conclusions: While statistically significant associations between changes in use patterns and changes in anxiety were not found in the present secondary study, adolescents with high baseline anxiety who reduce or abstain from cannabis may be more likely to experience anxiety reduction. This clinically important topic warrants further investigation among larger samples with additional power.
Financial Support: Supported by NIDA grants R01DA026777, R01DA042114, and R25DA020537

W25. Assessing Cannabis Use Disorder in Primary Care: Psychometric Performance of a Substance Use Symptom Checklist

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Drug Category Cannabis/Cannabinoids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Cannabis use disorder (CUD) is under-recognized in primary care. Brief, standardized assessment tools are recommended to help providers identify CUD but their psychometric performance is unknown. This study tests the psychometric properties of a Substance Use Symptom Checklist used in routine primary care among patients who report daily cannabis use.
Methods: Kaiser Permanente Washington screens adult primary care patients annually for cannabis use and administers a Substance Use Symptom Checklist (hereafter "Checklist") to patients who screen positive for daily use. The Checklist includes 11 items that assess substance use disorder (SUD) criteria defined in the Diagnostic and Statistical Manual for Mental Disorders, 5th Edition (DSM-5). Among patients who reported daily cannabis with no other drug use and completed the Checklist between March 2015-March 2020, item response theory (IRT) analyses tested whether the Checklist is unidimensional, discriminative, and reflects a continuum of CUD severity. Differential item functioning analyses examined whether the Checklist performs similarly across age, sex, race, and ethnicity.
Results: Among 16,140 patients who met inclusion criteria, 26.3% reported ≥2 symptoms on the Checklist, consistent with DSM-5 criteria for SUD. A unidimensional IRT model demonstrated excellent fit (comparative fit index=0.99) and indicated that Checklist items were able to discriminate substance use disorder severity. Differential item functioning was observed across age, sex, and race subgroups but had minimal impact on the total expected number of criteria (0-11) patients endorsed (i.e., differences in expected total criteria count for people with the same latent severity never exceeded half of one criterion).
Conclusions: A Substance Use Symptom Checklist, administered to primary care patients who report daily cannabis use as part of routine care, discriminated SUD severity and performed equally well across subgroups. Findings support the construct validity and clinical utility of the Checklist for identifying the spectrum of CUD in diverse populations.
Financial Support: National Institute on Drug Abuse, Clinical Trials Network (UG1DA040314)

W26. Delta-8 THC Use in US Adults: Sociodemographic Characteristics and Correlates

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Recent reports suggest a surge in the use of novel cannabis products whose primary active compound is Delta-8 tetrahydrocannabinol (Delta-8 THC). Nevertheless, little is known about the use of this novel cannabis product. We, therefore, examined patterns, sociodemographic characteristics, motivations, methods of consumption, and other Delta-8 THC use-related variables in a large online sample of US adult cannabis users.
Methods: Cannabis-using adult participants in a 2021 online survey (N=4,348) provided information on Delta-8 THC use, cannabis use, and sociodemographics. We used descriptive statistics to assess frequencies of sociodemographic covariates, patterns, and other correlates of Delta-8 THC. Logistic regression models estimated adjusted odds ratios (aOR) and 95% confidence intervals (CI) of the relationship between past 30-day Delta-8 THC use, sociodemographic characteristics, and other covariates.

Results: Among past 30-day cannabis users, 58% had heard of Delta-8 THC and 16.7% reported its use in the past 30 days. The most common consumption method was vaping concentrated formulations of Delta-8 THC (41.2%). Primary motivations for use were its legal status and perceived therapeutic benefits. Males were more likely than females to report past 30-day Delta-8 THC use (aOR= 1.4, 95% CI 1.18, 1.67). Delta-8 THC use was more common among younger ages, with the odds of use increasing monotonically with each decrease in age group. Respondents living in states with restrictions on sale of Delta-8 THC products had lower odds of Delta-8 THC use compared to those who lived with states without any restrictions (aOR=0.7, 95% CI 0.50, 0.86).
Conclusions: Findings provide initial insight into the current state of Delta-8 THC use in the US. There is an urgent need for further nationally representative data to investigate the correlates of Delta-8 THC use, such as the effectiveness of state-specific restrictions on its products. Such information can guide public health policy and legislation around Delta-8 THC use.
Financial Support: Funding is acknowledged from the National Institute on Drug Abuse and the New York State Psychiatric Institute (R01DA050032; T32DA031099; T32-DA037202; P30-DA037202).

W27. Marijuana Craving as a Predictor of Subjective Marijuana Effects

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Drug Category Cannabis/Cannabinoids
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: Marijuana is the most commonly used illicit drug in the United States. Craving is often assumed to lead to drug taking, but little is known about the effect of craving on subjective marijuana effects. This study aims to explore the prospective relationship of craving on subjective marijuana effects under different stress and drug-cue exposure conditions.
Methods: Participants (n=11; 5M; 37.5 ± 10 yrs) with moderate-severity Cannabis Use Disorder completed six sessions of a within-subject, placebo-controlled, crossover study that examined effects of yohimbine (0, 20, 40-mg oral), an □2-adrenoceptor antagonist that produces anxiety-like effects, and exposure to cues (neutral and marijuana-related) on choice to self-administer cannabis (6.0% THC; 0-11 puffs in a progressive ratio choice-task). Marijuana craving was measured using Visual Analog Scale items including, "I feel…" "an urge for marijuana," "a desire to use marijuana," and "a craving for marijuana." Subjective marijuana effects were measured using the Marijuana Rating Form, including "good marijuana effect," "bad marijuana effect," "strength of marijuana effect," "liking," "sedated," and "desire to take again." Number of marijuana puffs earned was recorded for all conditions.
Results: Linear regressions were used to explore whether session baseline craving scores predicted subjective marijuana effects in the six different stress/cue conditions. Preliminary results indicate that, after controlling for number of marijuana puffs smoked, baseline "craving for marijuana" was associated with "good marijuana effect" in the placebo yohimbine/neutral-cue condition ($t(1,6) = 2.59$, $p = .041$), and the 20-mg yohimbine/marijuana-cue condition ($t(1,6) = 3.01$, $p = .023$). Baseline "desire to use marijuana" was also associated with "good marijuana effect" in the 20-mg yohimbine/marijuana-cue condition ($t(1,6) = 2.54$, $p = .044$).
Conclusions: Baseline craving predicted subjective marijuana effects under different stress and drug-cue exposure conditions. These findings may indicate a cyclical relationship among craving, use, and subjective effects, furthering our understanding of mechanisms that underlie marijuana use.
Financial Support: NIH R21 DA040150 (LHL), Gertrude Levin Endowed Chair in Addiction and Pain Biology (MKG), Michigan Department of Health and Human Services (Lycaki/Young Funds)

W28. Mental Health and Life Events in Adolescents With Substance Use Disorders in the United States

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Drug Category Cannabis/Cannabinoids
Topic Health Services

Abstract Detail Human
Abstract Category Original Research
Aim: To examine the association between any substance use disorder diagnosis and recent mental health or life events among adolescent youth.
Methods: Data were analyzed from the 2020 National Survey on Drug Use and Health (NSDUH), an annual nationally representative survey of individuals 12 and older that provides data on the use of tobacco, alcohol, illicit drugs and mental health in the United States.
After accommodating for the survey's complex study design, we used logistic regression to evaluate the strength of the association between any substance use disorder (SUD) diagnoses, including alcohol, marijuana, vape use and other illicit use disorders, to major depression disorder (MDD) diagnosis, academic attendance, and arrests for an adolescent population of 12-17 year-olds. The prevalence for each SUD were reported along with the calculated odds ratios (OR) for the association between any SUD and each outcome.
Results: SUDs were associated with elevated rates of MDD and adverse life events. Sample included 5,723 adolescents where 3.5% had at least one SUD. Adolescents with a SUD had MDD at a rate of 38.2% as compared with 15.6% in controls (OR 3.5, 95% CI = 2.2 - 5.5). 38.7% of adolescents with a SUD skipped more than 1 day of school in the past 30 days as compared with controls with 26.3% (OR 2.3, 95% CI = 1.3 - 3.9). Adolescents with any SUD were more likely to have more than 1 arrest in the past year for breaking the law (10.8% vs 0.5%), (OR 22.3, 95% CI = 6.6 - 75.2). ORs increased in the presence of more than one SUD.
Conclusions: SUDs in adolescents were associated with higher odds of MDD and recent adverse life events. Clinicians can use these nationally representative data to stratify risks and direct to appropriate treatment when evaluating youth.
Financial Support: This project is supported by National Institute for Drug Abuse (NIDA) and the American Academy of Child and Adolescent Psychiatry (AACAP) Physician Scientist K12 award.

W29. Natural Reward Processing in Adults With Cannabis Use Disorder

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Drug Category Cannabis/Cannabinoids
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: Hedonic dysregulation – the overvaluation of drug reward relative to non-drug (i.e. natural) reward – is a core mechanism of drug addiction. However, there is a dearth of research on hedonic dysregulation among individuals with cannabis use disorder (CUD). As a first step, the current study tested the feasibility and initial efficacy of personalized scripted imagery to assess natural reward processing in adults with CUD.
Methods: Adults with CUD (n=10) and demographically matched non-CUD controls (n=12) completed a single-session personalized scripted imagery paradigm that included a natural reward script and a neutral script. Personalized scripts were presented in counterbalanced order, preceded by a standardized relaxation period, and approximately five minutes each. Primary outcomes included subjective (positive affect, craving), physiological (skin conductance), and neuroendocrine (cortisol) reactivity, and were assessed during and at 0, 5, 15, and 30 minutes post-script. Mixed effects models were used to compare between and within subject effects.
Results: There was a main effect of condition (natural reward vs. neutral) and group (CUD vs. non-CUD) on positive affect (PA), indicating greater overall PA during the natural reward script relative to neutral script (p=.006) and greater PA among non-CUD participants relative to CUD (p=.001). These effects were qualified by a significant interaction effect (p=.023) whereby CUD participants showed increased PA response during the reward script relative to neutral script (p=.001), while non-CUD participants did not differ within script type (p=.77). Overall cortisol response was lower in CUD participants compared to their non-CUD counterparts (p=.002). There were no significant effects of condition or group on skin conductance. Among CUD participants, there was no significant effect of condition on craving.
Conclusions: Adults with CUD may demonstrate deficits in natural reward processing relative to healthy controls. Personalized scripted imagery may be a feasible paradigm to assess and potentially remediate hedonic dysregulation in CUD.

Financial Support: NIH/NIDA K23DA045099 (Sherman), K24DA038240 (McRae-Clark); MUSC Department of Psychiatry internal funding (Sherman)

W30. Patterns of Substance Use and Mental Health Profiles Among Pregnant Women

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Drug Category Cannabis/Cannabinoids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: The overarching goal is to explore heterogeneity in substance use (tobacco and cannabis) and mental health symptoms (diagnosis, anxiety, depression) among pregnant women, and to investigate associations among class membership with age, parity, cannabis use at delivery and postpartum visit attendance.
Methods: Pregnant women presenting at an urban prenatal clinic in Baltimore, Maryland (N = 610) were assessed at initial prenatal visit, delivery and postpartum. Latent class analysis was used to determine the optimal number of classes based on five indicator variables, tobacco smoking, cannabis use, mental health diagnosis, anxiety symptoms, depression symptoms. Analyses quantified associations among class membership, background characteristics and distal outcomes.
Results: The optimal solution, based on numerous statistical indicators, suggested a three-class model of women including those characterized by (1) tobacco smoking, moderate probability of cannabis use and low probability of mental health problems, (2) no tobacco, moderate probability of cannabis use and high probability of mental health problems and (3) low probabilities on all variables. Women in classes 1 and 2 (cannabis use classes) compared to class 3 (low probabilities on all variables class), were significantly less likely to attend their postpartum visit (probabilities = .35 and .39, respectively vs. .57; Overall chi-square = 11.13, $p<.01$). Women in the cannabis use classes (classes 1 and 2) were significantly more likely to have used cannabis at time of delivery than women in class 3 (low probabilities on all variables class) (probabilities = .22 and .28, respectively vs. .05; Overall chi-square = 22.13, $p<.001$).
Conclusions: Heterogeneity exists in a population of women presenting at an urban prenatal clinic. Regardless of mental health status, women with moderate probabilities of cannabis use, were less likely to have a follow-up postpartum visit, suggesting cannabis use, even above risks indicative of tobacco smoking and mental health status, is associated with missed postpartum visits.

W31. Population Patterns Linking Adolescent Risk-Taking and Substance Use

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use typically begins during adolescence. Neurodevelopmental theories suggest adolescent substance use is driven by risk-taking behaviors that have lifespan peaks during this period. However, the generalizability of risk-taking-substance use linkages across the varied sociodemographic and health factors associated with real-world substance use, remains unknown. To inform the potential translation of adolescent risk-taking to large-scale, generalizable screening, prevention, and/or substance use intervention efforts, this project examined linkages between adolescent risk-taking propensity and cannabis and alcohol use across twenty-three sociodemographic, psychiatric, and health subgroups (spanning sex, race, socioeconomic status, community population density, religious affiliation, and mental and physical health strata).
Methods: National Survey on Drug Use and Health 2002-2019 data (N=1,005,421; 12-65-years-old) were used to fit non-linear lifespan trajectories (via spline regression) of composite self-reported risk-taking items (e.g., "[I] get a kick out of doing things that are dangerous") with statistical models that accounted for the complex survey design.

Results: Self-reported risk-taking propensity displayed a non-linear trajectory across the lifespan, with a robust peak during mid-adolescence (16.25 years-old) that matched neurodevelopmental predictions. While substantial average-level ("main effects") differences on risk-taking propensity were observed (e.g., males reported more risk-taking than females: Cohen's d = 1.22; low vs. high religious affiliation: d = 1.10), all twenty-three population subgroups displayed highly consistent peaks in risk-taking during mid to late adolescence (range across strata: 15.0 to 19.3-years-old). Risk-taking also consistently disambiguated daily adolescent cannabis users (range across strata: d's = 0.57 to 1.13) and alcohol users (range across strata: d's = 0.41 to 0.57) from non-users.
Conclusions: Analyses support neurodevelopmental predictions of adolescence as a period of heightened risk-taking that confers vulnerability to substance use. The consistency of adolescent peaks in risk-taking and links to regular cannabis and alcohol use across nearly all population subgroups, suggesting risk-taking measures may be useful in large-scale screening and related prevention efforts.
Financial Support: NIH K12 DA043490; American Psychological Foundation Visionary Grant

W32. The Reddit Cannabis Subjective Highness Scale: Applying Natural Language Processing to Inform Cannabis Use Measurement

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Drug Category Cannabis/Cannabinoids
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: With increasing cannabis legalization and emerging products available, there is a need for improved measurement of subjective effects of cannabis. The aim of this analysis is to apply natural language processing to social media textual data with corresponding self-reported numerical ratings of acute subjective highness following naturalistic cannabis use.
Methods: Titles were extracted via the Pushshift dataset from N=328,865 posts to a popular cannabis forum on the Reddit platform where posters self-assess and self-disclose how "high" they feel a scale from 1 to 10 (M = 6.9, SD = 1.8). Structural topic modelling was applied to identify frequently discussed topics and to examine the relationship between subjective highness rating and how often a topic appeared. The Linguistic Inquiry and Word Count (LIWC) dictionary was applied to identify text indicative of psychological processes in 6 categories (affective, social, cognitive, perceptual, time orientation, relativity). Linear regression examined associations between subjective highness rating and these psychological processes.
Results: The most frequent topics were characterized by references to smoking sessions, eager sharing of stories, and consumption of various foods and media. As subjective highness rating increased, people who posted were significantly more likely to discuss topics characterized by abstract observations, other people, and recent events, and to use words indicative of social and relativity processes; they were significantly less likely to discuss topics characterized by smoking locations, social references to subreddit members, and mellow positivity, and to use words indicative of affective and cognitive processes (all $p<.05$).
Conclusions: Text analyses reveal a broad range of contextual, social, affective, cognitive, and activity-based topics and psychological processes expressed by people rating and sharing their cannabis use experiences on Reddit. This formative subjective highness scale could be further developed and applied to self-assessments in behavioral pharmacology and ecological momentary assessment research settings.
Financial Support: NIDA K01DA046697, K25DA049944, R21DA048175

W33. Validity of DSM-5 Cannabis Use Disorder Severity Levels in Adults With Problematic Substance Use

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Drug Category Cannabis/Cannabinoids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research

Aim: The DSM-5 definition of cannabis use disorder (CUD) differs from DSM-IV cannabis dependence by including abuse criteria, withdrawal, and craving, but information on the validity of the DSM-5 CUD diagnosis and severity levels is lacking.
Methods: Study participants constituted a convenience sample of adult problem substance users, ≥18 years, recruited from two settings: a clinical research setting in an urban medical center and a suburban inpatient addiction treatment program. Participants who reported past-year cannabis use (n=396) consituted the sub-sample for this study. A semi-structured, clinician-administered assessment collected information on DSM-5 CUD criteria, cannabis use related variables, and psychopathology. For each validator (variable predicted to be related to CUD), regression models estimated whether the association with the validator differed by a binary diagnosis of DSM-5 CUD and with its severity levels.
Results: Binary DSM-5 CUD and CUD severity levels were associated with greater odds of cannabis use validators, including number of cannabis use days, self-reporting cannabis use as a problem, and cannabis craving scales. In addition, binary CUD and severe CUD were associated with co-occuring psychiatric disorders and social disfunction.
Conclusions: DSM-5 CUD and its dimensional measures were shown to have moderate validity, with severe CUD receiving the most support from its association with multiple validators across all domains, compared to the mild and moderate CUD measures associated with cannabis-specific validators alone. Further research is needed to determine the clinical utility of a mild DSM-5 CUD diagnosis among persons with problem substance use.
Financial Support: This work was supported by the National Institutes of Health (grant numbers R01DA018652 and 1R01AA025309) and the New York State Psychiatric Institute

W34. Cannabinoids in Plasma by LC-MS/MS: Application to Specimens From Youths With HIV

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Drug Category Cannabis/Cannabinoids
Topic Infectious Disease (e.g., HIV, HCV)
Abstract Detail Human
Abstract Category Original Research
Aim: To develop a sensitive LC-MS/MS method for the quantitative analysis of cannabidiol (CBD), its metabolites 7-hydroxy-CBD and 7-carboxy CBD, cannabinol, Δ9-tetrahydrocannabinol (THC) and its metabolites 11-hydroxy-Δ9-THC (11-OH-THC) and 11-nor-9-carboxy-Δ9-THC (THC-COOH) in human plasma and apply to authentic specimens from subjects in a study evaluating substance use in youths with HIV.
Methods: Specimens were obtained under the protocol, Consequences of Marijuana Use on Inflammatory Pathways in HIV-Infected Youth. Informed consent was obtained, and subjects were asked about marijuana and cannabidiol use. Blood specimens were obtained from twenty youth with HIV, 21-29 years old whose substance use profiles were known based on self-report. Blood was directly drawn into EDTA-containing vacutainer tubes; aliquots of double-centrifuged plasma were frozen and stored before analysis. Plasma samples (0.5 mL) were subjected to extraction and analysis by LC-MS/MS.
Results: No cannabinoids were detected in plasma of 7 subjects who reported either no cannabis use or intermittent / infrequent use (≤ once per month). Two subjects reported regular cannabis use (≥ once a month and ≤ once a week) but no drugs were detected. Eleven subjects were positive for THC, 11-OH-THC and/or THC-COOH; 7 of those reported daily use, one reported regular use, one reported no cannabis use and the self-report of 2 subjects was not given. Two of the eleven subjects were also positive for 7-carboxy-CBD; one reported no CBD intake and one unknown. One subject reported regular CBD use, two reported infrequent use of CBD, but none were positive for CBD or metabolites.
Conclusions: An LC-MS/MS method was developed and applied to analysis of plasma specimens for cannabinoids. CBD is heavily marketed to the cohort in the study, but results suggest there was not widespread use of CBD. There was some agreement with drug use self-report in this population, but biological specimen analysis provided more reliable data.
Financial Support: NIH grants 5R01 DA031017-05 (JWS, MMG), U01DA044571 (JWS) and Intramural Research Program of the NIAID

W35. Cannabis Predictors of Neurocognitive Outcomes in Adolescents and Young Adults After 3-Week Abstinence Period

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Drug Category Cannabis/Cannabinoids
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: Regular cannabis use during adolescence and young adulthood has been associated with poorer cognitive performance; however, research has primarily examined the effects of past year or lifetime cannabis use or has examined group differences (cannabis users versus controls). Limited research has examined how different markers of cannabis use (e.g., cannabis use disorder (CUD) symptoms) relate to cognitive performance. The current study aims to examine how other predictors of cannabis use patterns are associated with cognitive performance in adolescents and young adults after a three-week abstinence period.
Methods: 50 cannabis users (ages 15-26, 43% female, 63% non-Hispanic White) completed a neurocognitive battery after a three-week period of abstinence. Cannabis use variables were measured using the Customary Drinking and Drug Use Record and Timeline Followback interview. A stepwise regression was conducted to examine the relationship between cannabis use variables (i.e., past year and lifetime cannabis use, CUD symptoms, age of regular onset, and length of abstinence) and cognitive outcomes including Delis-Kaplan Executive Functioning System (DKEFS) trail making (condition 4: switching/inhibition) and color-word (inhibition condition); Wisconsin Card Sort Test (total cards); Ruff 2 and 7 (total accuracy and speed); California Verbal Learning Test-II (long delay free recall and total recall); and PASAT total score while accounting for covariates (i.e., sex, past year alcohol use, cotinine levels).
Results: For DKEFS Trails Condition 4, past year cannabis use was related to poorer performance (b= -.003, p= .004). Lifetime cannabis use was related to better total performance on the PASAT (b= .016, p= .03). Other findings were nonsignificant.
Conclusions: In this small sample of cannabis users, beyond past or lifetime cannabis use, no other markers were a robust predictor for neurocognitive performance after abstinence. Larger, longitudinal samples examining adolescent trajectories of substance use are needed to better disentangle the relationship between more complex cannabis use markers and neurocognitive outcomes.
Financial Support: Supported by: R01 DA030354 and U01 DA041025

W36. Chronic Oral Dosing of Cannabidiol (CBD) With And Without Low Doses Of Delta-9-Tetrahydrocannabinol (THC)

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: Determine the behavioral pharmacology and toxicology of repeated oral cannabidiol (CBD) administration with and without low doses of delta-9-tetrahydrocannabinol (THC) that approximate levels likely to be found in “full-spectrum” retail hemp products.
Methods: Eight healthy adults were randomized to self-administer 1mL medium-chain triglyceride (MCT) oil that contained either 100mg CBD (N=1), 100mg CBD + 2.8mg THC (N=3), or 100mg CBD +3.7mg THC (N=4) twice daily for 14 days. Synthetic CBD and THC were dissolved into MCT oil to create drug products. Initial dose exposure occurred during an 8-hr laboratory session during which subjective drug effects, vitals and cognitive performance were assessed and blood, urine, and oral fluid were collected for analysis. Outpatient dosing (14 days) was monitored via video surveillance and additional assessments collected during brief visits on Days 2, 7, 14, and 21 (1-week washout).
Results: Participants consistently reported mild subjective drug effects mostly characterized by decreased arousal in the two drug conditions that contained THC and an increase in appetite and dry mouth in the

100mg CBD + 3.7mg THC condition. Oral fluid testing consistently showed positive test results (4ng/mL THC cutoff), but only for samples obtained within 3 hours of dosing. Immunoassay testing of urine specimens (N=5) showed positive results at a screening cutoff of 50ng/mL THCCOOH for all 4 participants receiving THC, but not for the participant taking only CBD. None of the urine samples obtained after the 1-week washout (Day 21) were positive. Remaining urine and all blood samples are pending analysis.
Conclusions: Acute and chronic administration of MCT oil containing 100mg CBD, with and without small doses of THC, produced modest subjective drug effects, but did not robustly impact cardiovascular or cognitive endpoints. Exposure to THC resulted in positive urine immunoassay and oral fluid drug test results.

W37. Health Conditions as Predictors of Longitudinal Groups of Medicinal Cannabis Use During the Legalization of Recreational Cannabis in Los Angeles

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: California legalized recreational cannabis in 2016; yet, little is known about changes to medicinal cannabis use in the new policy environment. This study examined an association between lifetime chronic health conditions and longitudinal groups of medicinal cannabis use among young adults in Los Angeles between 2014-2020.
Methods: 366 cannabis patients and non-patients (aged 18-26 at baseline, 34% female) reported health and cannabis use during 6 waves of annual surveys. Groups were derived from a combination of documented medical cannabis patient status (yes/no) with self-reported primarily or exclusively medicinal (versus recreational) cannabis use using parallel-process latent class growth analysis. Lifetime chronic health conditions collected at baseline were estimated as predictors of class membership, accounting for age, Hispanic ethnicity, and sex assigned at birth.
Results: Three trajectory classes emerged. Class 1 (low-medicinal non-patients, 44.4% of the total sample) represented participants with low self-reported medicinal use and low-decreasing patient status. Class 2 (low-medicinal patients, 34.3%) was marked by low self-reported medicinal use and high-decreasing patient status. Class 3 (high-medicinal patients, 21.3%) was characterized by consistently higher self-reported medicinal use and high-decreasing patient status. Lifetime insomnia predicted membership in the patient groups (Class 2, $p<0.05$, and Class 3, $p<0.001$) relative to the non-patient group (Class 1). Lifetime spinal/musculoskeletal, neurological, and chronic pain conditions predicted membership in high-medicinal group (Class 3) compared to the other groups.
Conclusions: Legalization of recreational cannabis significantly reduced the demand for maintaining cannabis patient status among young adults. Yet, self-reported medicinal use remained consistent within groups across time. High probability of cannabis patient status in the pre-legalization period was associated with lifetime insomnia, regardless of self-reported medicinal use. High probability of self-reported medicinal use over time was associated with pain/neurological conditions at baseline. Future studies need to assess whether self-reported medicinal use contributes to improvements in chronic diseases among young adult cannabis users.
Financial Support: NIDA grants 1R01DA034067, 1R01DA034067-S1, 2R01DA034067

W38. Impaired Behavioral Insight During a Probabilistic Drug Vs. Non-Drug Reinforcer Choice Task in Severe Cannabis Use Disorder: Associations With Cannabis-Related Problem Awareness and Motivation to Change

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Drug Category Cannabis/Cannabinoids
Topic Behavior

Abstract Detail Human
Abstract Category Original Research
Aim: Compromised clinical insight in addicted populations is thought to decrease motivation to change, but empirical scrutiny has been limited. One component of insight is accurate self-monitoring of choice behavior when drug-related and alternative reinforcer options are available. Previous studies have found impaired behavioral insight during a probabilistic drug vs. non-drug reinforcer choice task in cocaine and opioid user populations. Here we present results from this task adapted for cannabis users, along with relationships between insight and change factors.
Methods: Non-treatment seeking individuals with severe Cannabis Use Disorder (CUD) (n=31) and non-cannabis-using controls (n=20) of both sexes completed a probabilistic behavioral choice task to assess preference for viewing pleasant, unpleasant, neutral, or cannabis pictures. Participants were asked which picture type they selected most, which was compared to task performance as an index of behavioral insight. The CUD group also completed self-report measures of problem awareness and motivation to change. A general linear model was created with the between-group factor group and the within-subject factor picture type. Insight and problem awareness/motivation to change were examined with a Chi-square test and analysis of variance, respectively.
Results: As predicted, results showed a significant group-by-picture type interaction, $F(3,47)=7.39$, $p<0.001$, $\eta2=0.32$, driven by more cannabis picture, $t(49)=3.56$, $p=0.001$, and fewer pleasant picture, $t(49)=-2.18$, $p=0.03$, selections by the CUD group compared to controls. The CUD group showed a greater proportion of impaired insight individuals compared to controls, $\chi2(1,n=51)=5.10$, $p=0.02$. Finally, individuals with CUD and intact insight reported more awareness of cannabis use-related problems, $F(1,29)=4.60$, $p=0.04$, $\eta2=0.14$, and greater motivation to change their cannabis use, $F(1,29)=4.20$, $p=0.05$, $\eta2=0.13$, than those with impaired insight.
Conclusions: Results were consistent with theory on insight and motivation to change. Behavioral insight on the probabilistic choice task may have utility for tracking motivation to change and/or as an intervention target for increasing treatment engagement in CUD.

W39. Medical Cannabis Use During Peri- And Postmenopause: A Survey Study

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Drug Category Cannabis/Cannabinoids
Topic Alternative Medicine
Abstract Detail Human
Abstract Category Original Research
Aim: Medical cannabis (MC) treatment is expanding throughout the US, with older adults representing the fastest growing group of consumers. However, limited research thus far has examined MC use to address menopause-related symptoms.
Methods: Respondents were recruited to participate in an online survey study through online postings focused on groups related to women's interests, women's health, and cannabis and cannabinoids. Respondents (perimenopausal n=131; postmenopausal n=127) completed the Day-to-Day Impact of Vaginal Aging Questionnaire (DIVA), Menopause-Specific Quality of Life Questionnaire (MENQOL), and the Arizona Sexual Experiences Scale (ASEX) to assess menopause-related symptomatology, and also provided information about general cannabis use and MC use for menopause-related symptoms.
Results: Across all respondents, the most burdensome menopause-related symptoms were sleep disturbance, fatigue, and lack of energy. Additionally, perimenopausal respondents reported significantly worse menopause-related symptomatology on the MENQOL ($ps\leq.037$) but not the DIVA or ASEX compared to postmenopausal respondents. Most respondents reported current cannabis use (86.1%) and endorsed using MC to treat menopause-related symptoms (78.7%). The top three menopause-related symptoms respondents reported using MC to treat were sleep disturbance (67.4%), mood/anxiety (46.1%), and libido (30.4%). Interestingly, perimenopausal respondents reported higher incidence of depression ($p=.025$) and anxiety ($p=.003$) as well as increased use of MC to treat menopause-related mood and anxiety symptoms relative to postmenopausal respondents ($p=.011$), suggesting that mood and anxiety symptoms may be a salient target for cannabinoid-based therapies that may be particularly problematic during perimenopause.
Conclusions: Many individuals are currently using commercially-available MC products as an adjunctive treatment option for menopause-related symptoms. Future research should examine the efficacy of specific

MC products, including assessing the impact of different cannabinoid profiles, modes of use, and other MC use characteristics on menopause-related symptoms. Results from this survey suggest that mood and anxiety symptoms are likely targets of interest for cannabinoid-based therapies, particularly in perimenopausal individuals.
Financial Support: Private donations to the Marijuana Investigations for Neuroscientific Discovery (MIND) Program

W40. Perceptions About Prenatal Cannabis Use in Postpartum Women With and Without a Personal History of Cannabis Use

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Drug Category Cannabis/Cannabinoids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Prenatal cannabis use is increasing, yet few studies assess women's perceptions regarding prenatal cannabis use. The present study compares perceptions of prenatal cannabis use among postpartum women with and without a personal history of cannabis use.
Methods: This secondary analysis uses data from an ongoing study of post-delivery women recruited from a postpartum unit. Participants completed an anonymous survey of demographics, substance use, and attitudes and beliefs about prenatal cannabis use. The present study compared perceptions about potential risks and benefits of prenatal cannabis use in women who never used cannabis (cannabis non-users; N=42) and those reporting current/past use (cannabis users; N=22). Data were analyzed using chi-square analyses and t-tests.
Results: Participants (N=64) were predominantly White (57.8%) with a mean age of 29.31 years. Two-thirds (65.5%) never used cannabis. For the current pregnancy, 14.1% reported first trimester use, and 10.9% reported third trimester use. Cannabis non-using women were more likely than cannabis using women to agree with 7 statements about adverse consequences of prenatal cannabis use. They included: having smaller baby (90.5% vs 54.5%, p=.02); affecting baby's brain (90.3% vs 64.3%, p=.034); affecting baby's development (94.1% vs 61.5%, p=.005); blocking nutrients to baby (73.1% vs 28.6%, p=.007); exposing baby to chemicals (94.3% vs 47.1%, p<.001); breathing problems (80.0% vs 23.1%, p=.001); and unsafe to use (88.9% vs 42.9%, p=.002). Cannabis using women were more likely than cannabis non-using women to agree with 3 statements about potential benefits of prenatal cannabis use. They included: increasing maternal appetite (100% vs 73.7%, p=.023); helping keep food down (100% vs 53.3%, p=.003); and okay to use (63.6% vs 13.3%, p=.001).
Conclusions: Cannabis using and non-using women differed in their perceptions of the outcomes of prenatal cannabis use, emphasizing the need for further research and education on the effects of prenatal cannabis use.
Financial Support: This research was supported by the VCU CCTR Endowment grant (Svikis PI) and the VCU CTSA grant (Jallo and Brown Co-PIs) UL1TR002649.

W41. Open Board

W42. The Estimated Effect of Prenatal Cannabis Exposure on Neonatal Birth Outcomes

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Prevalence of cannabis use among pregnant women in the United States (US) has doubled, and cannabis potency, measured by THC, has increased four-fold since the 1990s. Prior research findings on the relationship between prenatal cannabis exposure and neonatal birth outcomes are inconclusive. Here, I will build upon my findings presented at CPDD in June 2021. This year, I will investigate the association

between cannabis exposure and neonatal birth outcomes in a prospective cohort of pregnant women, with an increased sample size and updated methodology. Further, I hope to consider the shared variability between neonatal birth outcomes in relation to prenatal cannabis exposure.
Methods: The Michigan Archive for Research on Child Health (MARCH) prospective cohort of 606 women were recruited via probability-based sampling from 11 sites. MARCH gathered self-reports of cannabis use and covariates. Standardized neonatal outcomes included birth size, gestational age, preterm birth, 5-minute Apgar score, and neonatal intensive care unit admission. I estimated predictive associations using covariate-adjusted generalized linear models (i.e., maternal age, recruitment site, US census-based race/ethnicity, education level, tobacco smoking, and alcohol drinking).
Results: As estimated 15% of participants used cannabis while pregnant. An appreciable predictive association links prenatal cannabis exposure with modestly reduced birth size (approximate 95% confidence interval: -0.5, -0.01), but other prenatal cannabis exposure effect estimates are null. Work in progress includes multivariate modeling of neonatal outcomes.
Conclusions: Except for birth size, no appreciable prenatal cannabis exposure-associated differences in neonatal birth outcomes are observed in the current study. Limitations include omitted variables and constraints on statistical precision. Even so, women who are pregnant or might become pregnant should approach cannabis use with caution.
Financial Support: Michigan State University, NIDA 1R36DA054487-0, and NIDA 5R25DA051249

W43. Open Board

W44. Optimism Bias for Drug and Nondrug-Related Life Events in People With Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Abstract Detail Human
Abstract Category Original Research
Aim: People expect more good than bad to happen to them. This may be explained by a bias in cognitive and neural processes supporting belief updating, where favorable information about personal risk is weighed more strongly than unfavorable information. Although benefitting emotional well-being, this bias could inhibit preventive behaviors to mitigate future risk, potentially explaining, for example, why risky drug use can persist despite negative outcomes. Here, we adapted a well-validated framework and task to test for such a "domain-specific" optimism bias in opioid use disorder (OUD) and advance a computational understanding of the underlying cognitive process.
Methods: Chronic OUD patients (N=13) and matched controls (N=11) first estimated their likelihood of experiencing different drug use-related and nondrug-related negative outcomes (e.g., overdose, bone fracture). They then saw the actual base rate of each outcome for someone in their demographic, prior to re-estimating its likelihood again. Subjects were incentivized to be as accurate as possible in their estimates, which could earn them a bonus. For each person, we assessed how much likelihood estimates changed as a function of having received favorable vs. unfavorable information (first estimate-vs-base rate) and outcome type (drug/nondrug).
Results: Subjects updated their beliefs in a biased manner, revising their likelihood estimates of future negative outcomes more after receiving favorable compared to unfavorable information about their actual likelihood ($b=0.83$, $p<0.001$). This effect was stronger in patients ($b=-0.27$, $p=0.03$). In this preliminary sample, there were no additional modulatory effects of outcome type. However, patients tended to revise their likelihood estimates for drug-related outcomes less than nondrug-related outcomes after receiving unfavorable information ($b=-3.87$, $p=0.11$).
Conclusions: These data provide initial support for a domain-specific optimism bias in people with OUD and for a method to quantify this bias that could inform future neurobiological work aiming to link optimism bias to risky drug use decisions in this population.
Financial Support: This research is supported by grants from the National Institute on Drug Abuse (R01DA053282, PI: Konova; 2R25DA035161-06, PIs: Ruglass and Hien).

W45. Open Board

W46. Patient Perspectives on the Intersection of Social Relationships, Medication for Opioid Use Disorder, and the Criminal Justice System

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Persons with opioid use disorders (OUD) who are incarcerated face challenges upon re-entry into the community, including relapse to drug use and/or overdose. Those who decide to enter treatment and are receiving medication for opioid use disorder (MOUD) experience complex relationships with their social networks when they enter and leave the criminal justice system.
Methods: We interviewed 42 people receiving MOUD who had prior life experience with the criminal justice system to explore their relationships with family and friends to better understand the impact of these relationships on their recovery. A semi-structured interview guide explored five domains: 1) childhood experiences; 2) family reaction to entering prison/jail; 3) friends' reaction when sent to prison/jail; 4) family and friends' reaction upon release; and 5) treatment program staff reactions to knowledge of incarceration history. Interviews were digitally recorded and professionally transcribed. We applied a Thematic Analysis using an inductive and deductive coding framework to analyze the data.
Results: Five salient themes emerged from the data: 1) childhood experience with substance use among family and self were common and may have affected their own experience with substance use disorder although 2) some reported that their childhoods did not have these elements; 3) families, in general, especially a significant other (mother, grandmother) were saddened and upset when learning of their incarceration but remained supportive upon release; 4) family support waned on subsequent incarcerations, especially among more distant social network (other relatives and "friends"); 5) treatment staff were not judgmental/were supportive.
Conclusions: Despite describing that family relationships deteriorated over time, especially in the face of repeat incarcerations, these clients were receiving MOUD which may point to their resilience and is likely to promote their overall health well-being. Facilitating the maintenance of supportive relationships during incarceration and upon release may help with MOUD entry and retention.
Financial Support: This work was supported by APT Foundation, Inc.

W47. Post-Traumatic Stress Symptoms After Childbirth Among Women in Outpatient Treatment for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Posttraumatic stress after childbirth can negatively impact the well-being of the mother-infant dyad. Currently, no studies describe posttraumatic stress after birth among women with opioid use disorder (OUD). The postpartum period is a highly vulnerable time for this population, and posttraumatic stress after birth could trigger substance use and disrupt mother-infant bonding. The present study is among the first to characterize posttraumatic stress after birth among women in OUD treatment during the early postpartum period.
Methods: This a priori secondary analytic study uses longitudinal data investigating recovery among postpartum women receiving buprenorphine for OUD. Participants were enrolled during their third trimester of pregnancy and assessed within two weeks postpartum. For the primary outcome, women completed the PTSD Checklist-Civilian (PCL-C) with identification of the index trauma (an event that elicits clinically

significant posttraumatic stress response: e.g., childbirth, infant medical issue, a previous unrelated trauma). Postpartum PCL-C scores >29 identified posttraumatic stress after birth. Other Measures included: the Maternal Attachment Inventory (MAI), Perceived Control Childbirth scale (PCC), Brief Substance Craving Scale (BSCS), and satisfaction with labor and delivery pain relief.
Results: Participants (N=18) are predominantly White (72%) with Medicaid (73%). Eight participants (44%) met criteria for posttraumatic stress after birth and identified birth (n=2), an infant medical issue (n=3) or a previous unrelated event (n=3) as the index trauma. Participants with posttraumatic stress after birth reported relatively high levels of maternal attachment [mean MAI 28.1 (SD=4.8)] and perceived control in childbirth [mean PCC 51.1 (SD=12.9)]. Two participants reported opioid cravings, and three were dissatisfied with the level of labor and delivery pain relief.
Conclusions: Among postpartum women with OUD receiving buprenorphine, nearly half experienced posttraumatic stress symptoms after birth and 2/3rd attributed symptoms to a traumatic birth or infant medical issue. Findings highlight the importance of screening and trauma informed care in this population.
Financial Support: Training in the Pharmacology of Abused Drugs (PI: W. Dewey; T32DA007027), NIDA (PI: C.E. Martin; K23 DA053507), CTSA award UL1TR002649 from the National Center for Advancing Translational Sciences and VCU SOM VETAR grant

W48. Prescription Drug Monitoring Programs and Opioid-Related Arrests in the United States: Associations With Law Enforcement Agency Data Access and Operation in 1990-2016

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: The role of law enforcement in Prescription Drug Monitoring Programs (PDMPs) has evolved over time. By 2016, law enforcement agencies (LEA) gained PDMP data access in 44 states and DC, and operated PDMPs in six states. We examined associations between LEA-operated PDMP and LEA data access with synthetic opioid and opioid/cocaine arrest rates.
Methods: The 1990-2016 Uniform Crime Reporting Arrests data included 1,308,779 synthetic opioid and 10,195,855 opioid/cocaine arrests in 50 states and DC. Negative binomial regression with state random intercepts estimated associations of state LEA-operated PDMP and/or LEA data access with yearly state-level (a) total synthetic opioid arrest rates and (b) total other opioid/cocaine arrest rates, overall and by PDMP development phase (1990-1998, 1999-2004, 2005-2009, 2010-2016), adjusting for modern PDMP, census state covariates and time.
Results: In 1990-2016, average synthetic opioid arrest rates increased from 9.47 (95% CI=7.24-8.91) to 32.62 (95% CI=31.05-34.24) arrests/100,000 people. Other opioid/cocaine arrests decreased from 133.22 (95% CI=130.04-136.46) to 79.14 (95% CI=76.69-81.65) arrests/100,000 people. Synthetic opioid arrest rates were 111% higher in states with LEA-operated PDMPs (aIRR=2.11, 95% CI=1.27-3.51) than those operated by other agencies, and 47% lower in states with LEA data access (aIRR=0.53, 95% CI=0.38-0.72). The magnitude of these associations decreased over time (e.g., LEA-operated 1990-1998 aIRR=3.26 (95% CI=1.78-5.97), 2010-2016 aIRR=1.61 (95% CI=1.08-2.41)). There was no association between other opioid/cocaine arrests overall and LEA-operated PDMP (aIRR=0.76, 95% CI=0.53-1.07) or LEA data access (aIRR=1.13, 95% CI=0.92-1.40) overall or most PDMP phases, except for LEA data access in 1990-1998 only (1990-1998 aIRR=1.50, 95% CI=1.07-2.11).
Conclusions: States with LEA-operated PDMPs had twice the rate of synthetic opioid arrests in 1990-2016, with stronger effects in earlier PDMP development phases, while LEA data access was associated with lower synthetic opioid arrest rates overall. Associations were specific to synthetic opioids, not other opioids/cocaine excluded from PDMPs.
Financial Support: K01DA045224 (PI: Mauro), R01DA045872 (PIs: Cerda and Martins)

W49. Racial Differences in the Impact of Trauma on Opioid Misuse Among Justice-Involved Adolescents

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Drug Category Opiates/Opioids
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Systemic racism may be directly and indirectly associated with opioid misuse among justice-involved adolescents (JIA) through stress processes. The associations between race and trauma could possibly explain the recent stark increase in opioid deaths among Black individuals. Certain racial and ethnic minority groups are predisposed to potentially traumatic events and social stressors that exacerbate the effects of trauma. There is a deficit of research on how race and trauma impact risk for opioid misuse among JIA.
Methods: Stratified logistic regression was employed to analyze a statewide sample of 79,570 JIA from the Florida Department of Juvenile Justice (FLDJJ). This sample represented minors who were arrested for delinquency, completed the full intake assessment, and reached the age of 18 by the year 2016. Past 30-day OM was derived from self-reported data. Trauma was operationalized using the adverse childhood experiences instrument.
Results: More than 40% of the sample were Black adolescents, and over 90% of the sample experienced one or more forms of childhood trauma. The trauma items had cumulative and individual relationships with opioids, which varied across racial groups. Sexual abuse, family violence, and household substance misuse were associated with a 90% to 130% increased odds of opioid misuse. For one additional type of trauma experienced, the odds of opioid misuse increased by 27% among White JIA, 38% among Black JIA, 41% among Latinx JIA, and 36% among the total sample.
Conclusions: Initiatives that intend to resolve the opioid crisis may be improved by incorporating efforts to address trauma and the unique needs of certain racial and ethnic groups who are more susceptible to racial injustices.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

W50. Remifentanil Dose Ranging in Individuals With Physical Opioid Dependence and Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: This ongoing study seeks to determine the effects of a range of doses of the ultra-short acting opioid agonist remifentanil in individuals with moderate-to-severe opioid use disorder (OUD and physical dependence). The ultimate goal of this work is to identify appropriate remifentanil doses to be used in future self-administration studies. A previous study demonstrated that opioid-dependent subjects were more tolerant to remifentanil, but that study was conducted prior to the fentanyl epidemic and used a slow, constant infusion rate not representative of intravenous opioid abuse.
Methods: In the present study, subjects are admitted as inpatients and stabilized on oxycodone (40 mg, 4x/day) for a minimum of 7 days. Subjects then receive 3 remifentanil doses, with 40 deliveries of each dose administered by pump every minute over a 5-s infusion. To date, two subjects have received 0.03, 0.1 and 0.3 mcg/kg/infusion and two additional subjects received 0.1, 0.3 and 1.0 mcg/kg/infusion. Subjects complete drug-effect and street value questionnaires, and a capnography device provides continuous measurement of end-tidal carbon dioxide (EtCO2), respiration rate and percent oxygen saturation (SpO2). Data are analyzed using repeated measures linear mixed models. We hypothesized remifentanil would produce dose-dependent effects on opioid-sensitive outcomes, and the rapid dose delivery would be well tolerated.
Results: Remifentanil significantly increased EtCO2 ($p=0.007$) and ratings on certain subjective drug effect questionnaire items (e.g., Any Drug Effects, High, Good Drug Effects and Like Drug; $ps<0.05$), and

decreased SpO2 (p=0.004), typically as a function of dose. One subject exceeded dosing parameters (e.g., sedation, not requiring pharmacological intervention) at the highest (1 mcg/kg/infusion) remifentanil dose, but in general, the rapid delivery of these doses was well tolerated.
Conclusions: These preliminary results provide initial guidance for the use of intravenous remifentanil in human laboratory models of opioid abuse.
Financial Support: R01DA047368

W51. Responding to a Surge in Overdose Deaths: Perspectives From U.S. Syringe Services Programs

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: Overdose deaths in the U.S. have reached a record high. Syringe services programs (SSPs) provide multiple services addressing this crisis. This study examined SSPs' perspectives on factors contributing to the overdose surge, their response, and ongoing barriers.
Methods: From 2/11/2021-4/23/2021, we conducted 27 semi-structured interviews with U.S. SSP leadership and staff. Interviews were transcribed and qualitatively analyzed using a Rapid Assessment Process.
Results: Contributing factors: Respondents perceived that a large increase in fentanyl use, both alone and combined with other opioid and non-opioid drugs, was a major driver of the overdose surge. They also perceived that the COVID-19 pandemic increased solitary drug use and led to abrupt increases in use due to life disruptions and worsened mental health. SSPs' response: SSPs have increased naloxone distribution, including more doses per person (in case more are needed to reverse a fentanyl overdose) and expanding distribution to people using non-opioid drugs (in case these drugs contain fentanyl) and people who do not use drugs but could reverse overdoses as bystanders. Some are distributing fentanyl test strips, though a few expressed doubts about their effectiveness in reducing overdose harms. Respondents described adapting overdose prevention education to increase awareness of fentanyl risks, particularly when using non-opioid drugs. Ongoing barriers: Respondents expressed concern that SSPs are not sufficiently reaching certain groups at risk of overdose (e.g., people who use drugs without injecting). Many reported an inconsistent naloxone supply and difficulty obtaining nasal naloxone, which they perceived as easier to use than injectable naloxone. A few described having inadequate support from local public health leadership and law enforcement.
Conclusions: SSPs remain essential in preventing overdose death amid record numbers driven by increased fentanyl use and COVID-19-related impacts. Respondents reported multiple ongoing barriers. Increased resources and other supports for SSPs are urgently needed to successfully address this fatal and worsening crisis.
Financial Support: This work was supported by the Centers for Disease Control and Prevention (5 NU65 PS923685) and the National Institute on Drug Abuse (R01 DA027379 and K01 DA048172).

W52. Resumption of Methadone Following Release From Incarceration Delays Reincarceration for Any Cause in Men Eligible to Continue Methadone Treatment in Connecticut Jails

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: We aimed to estimate associations between receiving methadone treatment in jail, resumption of community-based treatment after release, and time until re-incarceration for men eligible to continue treatment in jail as part of a pilot program in Connecticut.
Methods: Retrospective case-control data on a sample of 1564 formerly incarcerated men in Connecticut, USA from 2014-2020 were used to test the hypotheses that receiving methadone treatment in prison and resumption of treatment in the community would be associated with longer time until re-incarceration for property, public nuisance, drug, or violent crimes. Accelerated Time Failure (ATF) Weibull models were used to fit survival distributions with exponentiated coefficients using Time Ratios (TR).
Results: Overall, 50.4% (n=788) were re-incarcerated with an average of 2.8 crimes (SD=1.0). Among those who were re-incarcerated, 36.4% (n=287) had charges for property, 32.0% (n=252) for public nuisance, 22.1% (n=174) for drug and 17.9% (n=141) for violent offenses. In Weibull models, receiving methadone during incarceration was insignificantly associated with time until re-incarceration for any of the crime types. Resuming methadone in the community was associated with longer time until re-incarceration for all crime types (TR=1.3, 95%CI, 1.1, 1.6, p<0.001). When examined by crime type, resuming treatment in the community was associated only with drug crimes (TR=1.4, 95%CI=1.2, 1.7, =<0.001) but not any of the other offenses. Resuming treatment more quickly was associated with greater time until re-arrest for any drug related crimes (TR=1.1, 95%CI=1.0, 1.1, p=0.033). African-American race was associated with shorter time until re-arrest for drug crimes compared to their white counterparts (TR=.6, 95%CI=0.4, 0.8, p<0.001).
Conclusions: Findings from this study underscore the importance of providing timely access to community-based methadone treatment following release from incarceration as a strategy to reduce risk of re-incarceration among people with opioid use disorders.
Financial Support: NU1ROT000012 R25037190 T32019426

W53. Retention on Treatment and Mortality of Opioid Use Disorder Patients After Methadone Take-Home Dosing Policy Change During COVID-19 Pandemic in Ukraine

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Original Research
Aim: To assess the effect of the expansion of methadone maintenance treatment (MMT) take-home dosing, implemented due to the COVID-19 pandemic, on retention and mortality of patients with opioid use disorder (OUD) in Ukraine.
Methods: A prospective quasi-experimental Kaplan-Meier survival analysis was applied to compare MMT retention and mortality between OUD patients enrolled in treatment during the year before the take-home dosing regulation update (March 18th, 2020), induced by COVID-19 restrictions, and those enrolled during the year following the policy change. Predictors such as age, sex, HIV status, methadone dosing, take-home dispensing, and previous MMT experience were assessed for their effect on treatment retention and death using Cox multivariate regression models.
Results: Among the pre-(N=3,350) and post-(N=3,775) COVID policy change cohorts, 26% and 55% of patients were transferred to take-home dosing within a year, respectively. Patients enrolled in post-COVID had significantly (p<0.0001) higher retention at 1(98% vs. 96%), 3(93% vs. 90%), 6(89% vs. 84%) and 12(82% vs.78%) months respectively; and higher (p<0.0001) survival probability at at 1(99.6% vs. 99.2%), 3(98.9% vs. 97.2%), 6(97.6% vs. 96.8%) and 12(97.9% vs. 95.1%) months, respectively. Patients enrolled post-COVID had a 29% lower risk for dropout over the entire 12 months (p<0.0001), controlling for age, sex, methadone dose, HIV status, and previous MMT experience. Similarly, the post-COVID group had a 30% lower risk of death (p=0.03) at 6 and 12 months, controlling for methadone dose and HIV status. MMT retention and patient mortality didn't differ after controlling for take-home dosing, indicating that take-home dosing is significantly associated with higher treatment retention and survival in a post-COVID group.
Conclusions: The proportion of patients transferred to take-home dosing during the post-COVID period was more than double that of the pre-COVID period. Take-home dosing contributed to higher retention and survival in the post-COVID group at 6 and 12 months.

Financial Support: R01DA033679

W54. Risky Alcohol Use Among Patients Dispensed Opioid Medications: A Clinical Community Pharmacy Study

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Background. Among the significant risk factors for opioid overdose is concomitant use of other central nervous system depressants, particularly alcohol. Given the continued expansion of community pharmacy in the continuum of care, it is imperative to characterize alcohol use among pharmacy patients dispensed opioids in order to establish a foundation for identification and possible intervention in these settings.
Methods: Methods. This secondary analysis utilized data from a one-time, cross-sectional health assessment conducted among patients dispensed opioid medications in 19 community pharmacies in Indiana and Ohio. Adult, English speaking, patients not receiving cancer care who were dispensed opioid medications were asked to self-report alcohol and substance use, behavioral and physical health, and demographic information. Descriptive statistics and logistic regression analyses were employed to identify patient characteristics associated with alcohol use/risky alcohol use.
Results: Results. The analytical sample included 1,494 individuals. Participants were on average 49 years of age (Standard Deviation=14.9)—with 6% being persons of color. Weekly drinking was reported by 18.1% and daily drinking was reported by 6.8% of the study sample, with 9.6% participants of reporting moderate/high risk drinking. Males (Adjusted Odds Ratio [AOR]=1.94, 95% CI=1.3,2.9), those with higher pain interference (AOR=1.44, 95% CI=1.0,2.0), overdose history (AOR=1.93, 95% CI=1.1,3.5), sedative use (AOR=2.11, 95% CI=1.3,3.5), and tobacco use (AOR=2.41, 95% CI=1.6,3.7) had greater likelihood of moderate/high risk alcohol use (all $p<0.05$).
Conclusions: Conclusions. Medication labeling and clinical guidelines clearly indicate that patients should abstain from concomitant of opioids and alcohol. This study has identified rates and associated risk factors of risky alcohol use among a clinical sample of community pharmacy patients dispensed opioid medications. Continuing this line of research and potential clinical service development has the ability to improve community pharmacy patient safety through addressing a significant gap within the current opioid epidemic.
Financial Support: This study was supported by the National Institute on Drug Abuse (UG1DA013732; UG1DA049444) and by the NIH Helping to End Addiction Long-Term (HEAL) Initiative.

W55. Substance Use Patterns and Self-Ascribed Masculinity/Femininity Among Incarcerated Women With a Recent History of Opioid Misuse

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Research and theory have indicated that both biological sex and the social construct of gender have an important impact on the initiation, trajectory, and recovery/remission of substance misuse. However, few studies have examined gender as a continuous construct as it relates to substance use.
Methods: Incarcerated women (N=125) were randomly selected from jail rosters, screened for a history of recent opioid misuse, consented to participate, and interviewed by research staff. All data were collected as part of the NIDA-funded Justice Community Opioid Innovation Network (JCOIN). Measures included sociodemographic information, recent and lifetime substance use, and the Traditional Masculinity-Femininity (TMF) Scale, a 6-item instrument measuring central aspects of self-ascribed masculinity and femininity (e.g., attitudes/beliefs, interests, appearance, or behavior) on a 7-point scale (1=very masculine, 7=very feminine).

Results: All participants reported female sex at birth and self-identified their gender as female. Bivariate correlations were used to examine relationships between substance use and individual TMF items, a total sum TMF scale score (M=29.4, SD=8.2, range=6-42), and a calculated standard deviation (SD) score measuring variation across item responses. Women who rated their interests as more feminine were older ($r=.18$, $p<.05$) and had later initiations for illegal drug use ($r=.18$, $p<.05$) and regular/problematic drug use ($r=.20$, $p<.05$). Women who had a lower SD score (more consistent responses) initiated alcohol use later ($r=-.23$, $p<.05$) and were older ($r=-.18$, $p<.05$). Women who rated their behavior as more feminine also reported later alcohol initiation ($r=.20$, $p<.05$).
Conclusions: Even in a sample of only women (in both sex and gender identity), participants exhibited considerable differences in self-ascribed masculinity and femininity. Results suggest that participants who identify as more traditionally feminine may have lower-risk substance use profiles. Future research should further investigate variations in substance use, related risk behaviors, and treatment as a function of self-ascribed masculinity and femininity.
Financial Support: This study was supported by the University of Kentucky (UG1DA050069) research hub of the NIDA JCOIN cooperative agreement.

W56. The Association Between Exercise and Opioid Misuse: A Systematic Review

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Literature Review
Aim: Exercise releases endorphins in the brain and improves health outcomes. This review aimed to summarize the existing literature on the association between exercise and opioid misuse in observational and experimental studies.
Methods (Optional): Studies will be identified by searching five databases up until December 2021 and independently assessed for inclusion by two authors. Studies conducted among adults aged 18 years or older were included and those assessing heroin use or conducted among pregnant women or institutionalized individuals were excluded. The risk of bias and quality assessment was conducted independently by two authors, using the NIH Study Quality Assessment Tools. All decisions were cross-checked and discussed where necessary with a third author.
Results (Optional): A preliminary search using one database (PubMed) yielded 178 records, of which 10 studies were included. Eight studies used self-reported measures of opioid misuse. Four studies were pilot trials, two were randomized controlled trials, two were case-control studies, and two were cross-sectional studies. Six studies evaluated engagement in yoga and four studies evaluated engagement in exercise or sports such as college athletics, synchronized swimming or dance sports. Five of the findings claimed that there was no statistically significant association between exercise and opioid misuse. Reductions in opioid misuse were found among individuals practicing yoga or those with baseline opioid use. Increases in opioid misuse were found among young adults participating in organized college-athletics.
Conclusions: Overall, evidence from observational and experimental studies was mixed. Future researchers interested in the association between exercise and opioid misuse should consider large samples of participants with standardized questions on opioid use and could potentially use randomized controlled trials.
Financial Support: Supported by the National Institute on Drug Abuse of the National Institutes of Health [Award Number R25DA051249]

W57. The Association Between Physical Therapist Advanced Orthopaedic Certification and Their Attitudes About Prescription Opioid Medication Misuse Management Practices: A Cross-Sectional Study

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Drug Category Opiates/Opioids
Topic Health Services

Abstract Detail Human
Abstract Category Original Research
Aim: Physical therapists (PTs) are often confronted—and may be able to address and manage—patients with prescription opioid medication misuse (POMM). Effective management of patients with POMM requires therapeutic commitment to those patients. Some PTs have advanced orthopaedic physical therapy credentials such as the orthopaedic certified specialist (OCS) or the orthopaedic subspeciality credential of Fellow of the American Academy of Orthopaedic Manual Physical Therapists (FAAOMPT). The purpose of this study was to evaluate the association between holding OCS or FAAOMPT credentials and PTs' perceptions about working with patients engaging in POMM.
Methods: A national web-based survey of PTs inquired and identified whether respondents had an OCS or FAAOMPT credential. PTs' perceptions were assessed using a modified 20–item Drug and Drug Problems Perception Questionnaire (DDPPQ). Linear regression evaluated the association between credential status and each DDPPQ subscale (role adequacy, role legitimacy, role self-esteem, role support and job satisfaction).
Results: The analysis included 402 respondents with a mean age of 41.0 (SD=11.2). There were 91 (22.6%) FAAOMPTs, 143 (35.6%) OCSs with no FAAOMPT credential and 168 (41.8%) had neither credential. Having an FAAOMPT credential was associated with more favorable perceptions of role support (b =-1.42, 95%CI =-2.73 to -0.12) and job satisfaction (b=-1.33, 95%CI =-2.46 to -0.23) than those with an OCS credential only. Compared to those with neither credential, the FAAOMPT credential was associated with more favorable perceptions of role self-esteem (b =-1.42, 95%CI =-2.59 to -0.26) and job satisfaction (b =-1.38, 95%CI =-2.52 to -0.25). PTs with an OCS credential did not report more favorable POMM-related perceptions that those without an OCS or FAAOMPT credential for any DDPPQ subscale.
Conclusions: Obtaining the FAAOMPT credential may lead to more favorable perceptions in several POMM-related patient management domains. Research is needed to determine why FAAOMPTs report more favorable POMM-related perceptions.
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W58. Training, Development, and Implementation of Novel Peer Support Led Programs for Persons With Opioid Use Disorder (OUD)

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Program Descriptions
Aim: The HEALing Communities Study (HCS) in Kentucky developed two Peer Support Specialist (PSS) programs to support the main study goal of decreasing opioid-involved overdose deaths. The linkage program aims to connect individuals with OUD to medication treatment (MOUD). The retention program aims to help participants overcome barriers to support MOUD treatment retention. The goal herein is to describe the training strategies, development, and early implementation outcomes of these programs.
Methods (Optional): As prerequisite training, all peers are certified adult PSS in substance use disorder (SUD), trained in recovery coaching and recovery capital assessment, crisis response, and SMART and SMART Family and Friends support meetings, which requires 110 training hours. Additional linkage and retention program training was developed using pre-existing webinars from the Provider Clinical Support System and novel training created by HCS faculty SUD experts in conjunction with PSS partner agencies.
Results (Optional): This novel linkage and retention program training resulted in an additional 69 training hours over many topic areas, including motivational interviewing, basics of SUD/OUD and how and why MOUD works, overdose education and naloxone distribution, and documentation and data collection.

Trainings are in-person and by webinar, small group and 1:1. They have been revised with peer and community partner feedback as implementation proceeds in the field. To date 23 peer support navigators are deployed/planning for deployment in 31 community agencies. 298 individuals have participated in linkage, and 218 have enrolled in retention programs.
Conclusions: We developed a robust and comprehensive training plan for PSS working to help link and retain individuals in MOUD. Program development required and benefited from strong community partnerships with ongoing feedback, supporting successful initial implementation in the field.
Financial Support: This research is supported by the National Institutes of Health through the NIH HEAL Initiative under award number UM1DA049406 and the Substance Abuse and Mental Health Services Agency under award number H79TI083283. Opinions expressed are those of the authors and do not represent the position of the National Institute on Drug Abuse or SAMHSA. The authors have no relevant conflicts of interest to report.

W59. Open Board

W60. When Everyone's a Critic: How Social Factors Impact Individuals With Opioid Use Disorder and Influence Treatment Engagement

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Medications for opioid use disorder combined with counseling and behavioral therapies are an effective treatment for opioid use disorder (OUD). However, opioid treatment engagement is an ongoing challenge with retention rates ~30-50%. Social factors have been identified as important to recovery, yet it remains unknown how social factors influence treatment engagement. Here, we aimed to characterize the social networks, relationships, and coping strategies of treatment-engaged individuals and longitudinally assess how these factors related to opioid reuse and treatment adherence.
Methods: We compared individuals receiving medications for OUD (N=62) and age, sex, and race/ethnicity matched controls (N=39) on a battery of self-report measures related to a) perceived social status, b) size, quality, and embeddedness of social networks, c) social wellbeing (perceived support vs. criticism), and d) social coping strategies. We then examined how these factors correlated with opioid use and treatment adherence over ~7 months, assessed by self-report and urinalysis.
Results: Individuals with OUD reported significantly lower perceived social status ($T=3.68$, $P<0.001$) and social network embeddedness ($T=2.03$, $P<0.05$) compared to control participants. Further, despite similar levels of perceived social support ($T=1.15$, $P>0.05$), OUD participants reported higher levels of perceived criticism ($T=2.93$, $P<0.005$) and utilized friend-related social coping strategies significantly less ($T=2.41$, $P<0.05$), relying more on prayer, a more solitary strategy ($T=2.71$, $P<0.01$). Importantly, OUD participants reporting higher perceived criticism used opioids in higher amounts ($Rs=0.39$, $P<0.01$) and more frequently ($R=0.32$, $P<0.05$) during treatment. Conversely, those with higher social network embeddedness were more likely to attend therapeutic group meetings ($Rs=0.35$, $P<0.05$).
Conclusions: Supportive relationships are important for recovery; however, even with support levels comparable to that of controls, individuals with OUD perceive more criticism, which correlates with drug use. While support remains important to recovery, these findings shift the focus towards social network embeddedness and the impact of criticism as social factors influencing treatment success.
Financial Support: This work is supported by NIH/NIDA (R01DA053282, R01DA054201) and NJ Alliance for Clinical and Translational Science TL1 Fellowship.

W61. Open Board

W62. "I'm Clean And Sober, But Not Necessarily Free:" Motivations To Discontinue Treatment Among Patients On Long-Term Buprenorphine

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Drug Category Opiates/Opioids
Topic Health Services
Abstract Detail Human
Abstract Category Original Research
Aim: Patients receiving buprenorphine for the treatment of opioid use disorder (OUD) experience a roughly 50% reduction in mortality risk relative to those not receiving medication. Longer periods of treatment (>15 months) are also associated with improved clinical outcomes. Despite the benefits, most patients discontinue buprenorphine prematurely. This study aimed to examine patient motivations for discontinuation, which may inform clinical interventions to support retention in treatment.
Methods: This study was conducted at the VA Portland Health Care System (2019-2020). Participants must have received buprenorphine for the treatment of OUD for ≥2 years. Qualitative interviews lasted 30-60 minutes, were audio recorded and transcribed verbatim. Coding and analysis were guided by directed qualitative content analysis.
Results: Fourteen patients engaged in office-based buprenorphine treatment completed interviews. Patients expressed strong enthusiasm for buprenorphine as a medication, calling it, "a miracle drug" and "a blessing" that had, "saved my life." Nonetheless, the majority expressed the desire to discontinue, including 3 patients actively tapering. Motivations to discontinue fell into four primary categories. First, patients were troubled by perceived side effects of the medication, including effects on sleep and dreams, emotion, sex drive and memory. Second, patients expressed unhappiness with being "dependent" on a medication, which was framed in opposition to personal strength and independence. Third, patients expressed stigmatized beliefs about buprenorphine, describing it as "addictive," "illicit," and associated with past drug use. Finally, patients expressed fears about buprenorphine unknowns, including potential long-term effects on the body, and interactions with medications required for surgery.
Conclusions: Despite overall satisfaction, patients engaged in long-term buprenorphine treatment express a strong desire to discontinue, often rooted in stigmatized beliefs about the medication. To encourage treatment retention, clinicians should inform patients of the risks of discontinuation, address and reframe stigmatized beliefs, and be prepared to answer health and clinical concerns.
Financial Support: This work was supported by the Agency for Healthcare Research and Quality (K12HS026370), the U.S. Department of Veterans Affairs Health Services Research and Development (1IK2HX003007) and resources from the VA Health Services Research and Development-funded Center to Improve Veteran Involvement in Care at the VA Portland Health Care System (CIN 13-404). Funders had no involvement in study design, data collection, data analysis and interpretation or writing of the abstract. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality, the United States Government or the Department of Veterans Affairs.

W63. A Comparison of Treatment Outcomes Between Women Receiving and Not Receiving Medication for Opioid Use Disorder From a RCT of CBT4CBT for Women in Residential Treatment

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Cognitive behavioral therapy and medication (e.g., buprenorphine) are evidence-based treatments for SUD that help reduce substance use recurrence. The present study aims to compare treatment outcomes between women receiving and not receiving medication for opioid use disorder (MOUD) using data from an RCT assessing adjunctive computer-based training for cognitive behavioral therapy (CBT4CBT) in residential treatment.
Methods: This is a secondary data analysis of a two-arm clinical trial comparing women randomized to either standard residential treatment plus adjunctive CBT4CBT or residential treatment alone (TAU). Because over half (54.5%) of the participants who completed the RCT were prescribed MOUD, women

receiving MOUD (n=24) and not receiving MOUD (n=20) were compared by treatment condition over the 12-week post-discharge follow-up period on recurrence of any substance (Y/N) and days of use using chi-square and t-tests respectively. Assessments included in analyses occurred at baseline and 12-weeks post-discharge from residential treatment.
Results: Participants (N=44) were primarily middle-aged (42.4±11.8 years), non-Latinx Black (79.5%), and single (70.5%). Most received SUD treatment prior to current treatment episode (84.1%). Nearly all women with opioid use disorder were receiving MOUD (92.3%). Women in the MOUD group tended to have more severe SUD evidenced by higher rates of polysubstance use, injection drug use, and prior overdose. Substance use recurrence rates were higher in the MOUD group (58.3%) than the non-MOUD group (30.0%). Within both the MOUD and non-MOUD groups, women in the TAU condition had higher median days of any substance use than those in the CBT4CBT condition [MOUD: 12 (range 4-56) vs. 3 (range 1-61); non-MOUD: 16 (range 10-48) vs. 1 (range 1-12)].
Conclusions: Differences in treatment outcomes by medication group may be due to higher SUD severity in the MOUD group. Findings were in the predicted direction with both CBT4CBT groups reporting fewer days of substance use than TAU.
Financial Support: This work was supported by Virginia Commonwealth University College of Humanities and Sciences Catalyst grant. NIDA T32DA007027 (PI: W. Dewey), NIDA K23 DA053507 (PI: C.E. Martin)

W64. A Novel Telehealth Model for Improved Retention in Opioid Use Disorder Treatment

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Drug Category Opiates/Opioids
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid use disorder (OUD) treatment via virtual care platforms promises to overcome barriers patients encounter including transportation, stigma, and related costs. COVID-19 reforms have waived requirements for in-person care allowing for innovation among startups as well as incumbent health systems. Virtual OUD care solutions now have a vast reach spanning all states. Given long-standing challenges in retaining OUD patients in traditional office-based buprenorphine treatment, we aimed to evaluate retention within a digital-first multi-state practice utilizing team-based virtual model of OUD treatment.
Methods: For this observational study we analyzed a sample of consecutive patients enrolled in treatment between July 1, 2020-December 31, 2020 with a 60+ day wash out period to identify new care episodes. Kaplan-Meier survival analyses were used to determine retention, with discontinuation being defined as 60+ days between clinical visits, consistent with precedent literature. We also performed a secondary analysis based on geography, grouping patients by USDA metropolitan v. rural/small town areas and compared patient locations to SAMHSA identified distributions of x-waivered prescribers.
Results: A total of 475 patients were included; 60.3% men, mean age 36.3 years (SD=7.1), the majority receiving Medicaid. Two-thirds (66.5%) self-reported race/ethnicity: 88.3% white, consistent with prior studies of buprenorphine maintenance patients with 78.1% residing in metropolitan areas and 21.9% in rural/small towns. The 180-day retention rate was 69.1% (95%CI:65.0-73.2%) with 71.0% (95%CI:66.4-75.6%) of patients in metropolitan centers retained at 180 days, versus 62.0% (95%CI:52.8-71.2%) in rural/small town areas ($\chi 2=2.62$, df=1, p=.105). A visual inspection of heat maps of patient residence by zip code showed that geographic variation of patient locations was much greater than that of x-waivered prescribers.
Conclusions: Findings demonstrate that telehealth for buprenorphine is effective across geographic regions and can exceed the physical reach of x-waivered clinicians. Retention rates were approximately double that of previously published studies of multi-state commercially insured and Medicaid populations.

W65. Addressing Barriers to Buprenorphine Treatment Among People Experiencing Homelessness: The Provider Perspective

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: People experiencing homelessness (PEH) bear a disproportionate burden of opioid-related deaths. Yet, little qualitative data exists about the barriers related to accessing buprenorphine treatment among PEH with opioid use disorder (OUD). This study sought the perspectives of service providers to understand the barriers and facilitators to buprenorphine access and stabilization among PEH with OUD at the patient, clinic, and structural levels. We also sought to identify recommendations for remediation.
Methods: We conducted in-depth Zoom interviews with service providers (n=28; 18 female identifying, 7 male identifying, and 3 identifying as transgender or nonbinary), including prescribing clinicians, pharmacists, outreach staff, and program managers in organizations providing care to PEH with OUD. Interviews were conducted from March to July 2021, and were audio recorded, transcribed, coded, and analyzed to identify major themes using thematic analysis.
Results: Patient-level barriers included patients' past negative experiences with buprenorphine and difficulties managing buprenorphine while unsheltered; recommendations for remediation included patient education, peer-to-peer education, and access to housing. Clinic-level barriers included clinicians' discriminatory attitudes toward PEH with OUD, lack of care continuity, and differing philosophical approaches to appropriate use of buprenorphine; recommended remediators included provider training and increased accessibility of buprenorphine in the community. Structural-level barriers included system-level care complexity, problems with patient identification and tracking, and lack of community resources; remediators included implementing medication delivery systems, pop-up pharmacies, and changes in identification requirements.
Conclusions: This study identified barriers to buprenorphine access and stabilization that are specific to the needs and circumstances of PEH. Findings provide recommendations for expanding existing services and for innovations at the level of patient care and health system delivery that are critically needed to respond to the opioid overdose crisis in this population.
Financial Support: This study was supported by a grant from the National Institutes of Health (R21DA050038 to C.L.M.).

W66. COVID-Related Distress, Coping Motives, and Substance Use Among Women With a History of Sexual Assault During the COVID-19 Pandemic

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use has increased among women in the United States during the COVID-19 pandemic and is associated with increased distress. Yet no research has examined links between COVID-related increases (CVI) in distress and substance use (CVI-SU) among women with a history of sexual assault and unhealthy drinking – a population at risk of developing substance use disorders. The present national cross-sectional survey hypothesized higher levels of COVID-related distress, alcohol coping motives, and polysubstance use among women reporting vs. not reporting CVI-SU.
Methods: Women (N=430, 83% White, 92% Non-Hispanic, 18% sexual minority) self-reporting a history of sexual assault ("have you ever had an uncomfortable or unwanted sexual experience?"), unhealthy drinking (Alcohol Use Disorders [AUD] Inventory Test-C>4), and no substance use treatment history completed an online survey. Rates of substance use, COVID-related increases (CRI) in distress, as well as coping motives for drinking and history of mental health treatment were examined among women reporting (n=164) vs. not reporting (n=266) CVI-SU ("During COVID-19, did you notice increased alcohol or other substance use?").
Results: Women reporting CVI-SU vs. no-CVI-SU indicated greater AUD symptoms ($p<.001$) and increased likelihood of cannabis ($p=.031$), tobacco ($p=.034$), and cocaine use ($p=.039$), as well as CRI-

distress (anxiety, depression, loneliness, frustration or boredom - all p's<.001) and coping motives for drinking (p<.001). The proportion of women who reported vaping, methamphetamines, and a history of mental health treatment did not differ by CVI-SU (p>.05).
Conclusions: Findings corroborate research linking COVID-related distress to increased substance use in women and extend this body of work to women at heightened risk of developing substance use disorders – women with a history of sexual assault victimization, unhealthy drinking, and no history of substance use treatment. COVID may have exacerbated distress and substance use in this trauma-exposed sample irrespective of prior mental health treatment.
Financial Support: NIH/NCCIH (3 U01 AT010863-02S1); NIH/NHLBI (T32 HL076134)

W67. Characteristics Associated With Opioid Misuse Among At-Risk Adolescents

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Adolescents in the criminal justice system are an understudied and underserved health disparity population that is particularly vulnerable to the opioid crisis. Adolescents in the justice system tend to experience more poverty, violence, family dysfunction, and mental health problems in their childhoods trauma than adolescents who never enter the system. There is a gap in the literature on which risk factors have the strongest association with opioid misuse. This information could help develop risk assessment instruments that are specific to this unique population.
Methods: Logistic regression was employed to investigate a state-wide sample of 79,960 JIA from the Florida Department of Juvenile Justice (FLDJJ). This sample includes all youth who (a) received one or more arrests for delinquency, (b) completed the full intake assessment, and (c) reached the age of 18 by the year 2016. Past 30-day opioid use was obtained from self-reported data. Several potential risk factors were examined.
Results: The factors with the strongest association with opioid misuse included: hopelessness, resistance to delinquent peers, leads delinquent activities, sexual abuse, family violence, household substance misuse, cumulative adverse childhood experiences, impulsivity, multiple substance use problems, and drug tolerance.
Conclusions: Justice-involved adolescents are predisposed to a barrage of risk factors, and a handful of these are strongly associated with opioid misuse. These data can be leveraged to design precise risk assessments to identify adolescents with eh greatest needs and provide them with the necessary care.
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W68. Circumstances and Correlates of Providing Assistance With Someone's First Injection in the AIDS Linked to the Intravenous Experience Cohort, Baltimore, MD

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Assisting with another individual's first drug injection has been reported by 13-70% of people who inject drugs. We aimed to describe prevalence, circumstances, and correlates of providing assistance with a first injection among people who inject drugs in Baltimore, MD.

Methods: All participants of a cohort of people who inject drugs in Baltimore, Maryland who had a study visit between September 2019 and March 2020 (n=848) completed a survey about assisting with another person's first injection. We characterized the prevalence of ever assisting, number of people assisted, reasons for providing assistance, and who the person assisted was. We also examined associations between measures of injection risk (hepatitis C infection, sharing syringes, shooting gallery attendance, and injection frequency) and ever providing assistance (vs. not) using logistic regression models adjusted for sociodemographic and substance use characteristics.
Results: Participants were primarily male (66.1%) and African American (82.9%), aged a median of 42 years, and injecting a median of 18 years. The 18.5% (n=157) of participants who had ever provided assistance during another person's first injection assisted a median of 2 people (IQR: 1-4). The most common reasons for providing assistance were because the person did not know how to inject (73.7%) and because the person shared drugs (44.9%). Participants reported assisting friends (58.0%), acquaintances (29.9%), and partners (21.7%). In multivariable models, ever having hepatitis C infection (OR [95% CI]: 2.5 [1.4-4.5]), sharing syringes (2.2 [1.2-3.9]), and injecting 3+ times per day (2.0 [1.2-3.4]) were associated with ever providing assistance.
Conclusions: Assisting with someone else's first injection was reported less frequently than most prior studies. The extent to which the stigmatized nature of assisting impacted reporting is unknown. These results emphasize the importance of considering a diverse set of reasons (i.e., economic, altruistic) and using a harm reduction framework in planning future interventions.
Financial Support: NIDA U01-DA-036297, R01-DA-053136, DP2-DA040256 and the Johns Hopkins University Center for AIDS Research (1P30AI094189).

W69. Contraceptive Use and Substance Use Disorder Treatment Utilization by Reproductive-Age Women Who Use Drugs in Rural Communities in the United States: A Cross-Sectional Survey

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Women who use drugs (WWUD) experience up to double the unintended pregnancy rate than the general U.S. population. Women in rural communities are increasingly using drugs. We estimated contraception use prevalence of WWUD in rural U.S. communities and tested associations between contraceptive use and recent substance use and substance use disorder (SUD) treatment.
Methods: The Rural Opioid Initiative (ROI) was a cross-sectional survey of people with recent non-prescribed opioid and/or injection drug use across eight rural U.S. regions. Recruitment occurred from January 2018 to March 2020 using respondent-driven sampling (RDS). We determined unweighted and RDS-weighted contraceptive use prevalence estimates amongst women (18 to 49 years old) who self-reported ability to conceive. Outcomes were prior 30-day opioid, methamphetamine/crystal, cocaine/crack, alcohol, or tobacco use and two SUD treatment categories 1) counseling, inpatient, or withdrawal program and 2) medication for opioid use disorder (MOUD). We used Chi-squared tests and multi-level linear regressions to test for associations.
Results: Of 855 ROI women, mean age was 33 (SD 8) years, predominantly White (83%), and insured (79%); 85% had recently used opioids and 73% methamphetamine. Participants reported 36.8% (95% CI 33.7-40.1) unweighted and 38.6% (95% CI 30.7-47.2) weighted contraceptive use. We found no association with contraceptive use and prior 30-day opioid, cocaine, alcohol, or tobacco use. However, women with methamphetamine use were 28% less likely to report contraceptive use than those without recent methamphetamine use (aOR 0.72 [95% CI 0.52, 0.99]). Contraceptive use was associated with counseling, inpatient, or withdrawal program (aOR 1.52 [95% CI 1.11-2.09]). There was a positive association with MOUD (aOR 1.34 [95% CI 0.95-1.88]) that did not reach the threshold for statistical significance.

Conclusions: WWUD in rural communities, particularly those using methamphetamine, reported low contraceptive use. Our findings highlight the need for expanded access to reproductive health and SUD services for WWUD in rural communities.
Financial Support: National Institute of Drug Abuse (NIDA), the Appalachian Regional Commission (ARC), the Centers for Disease Control and Prevention (CDC), the Substance Abuse and Mental Health Services Administration (SAMHSA), and Agency for Healthcare Research and Quality (AHRQ).

W70. Creation of a Simple Microsimulation Model for Assessing the Impact of Treatment on Opioid Misuse in North Carolina

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: The aim of this study is to develop a simple microsimulation model that can be used to quickly evaluate the effects of policy decisions on access to treatment for opioid misuse in North Carolina. By creating a flexible microsimulation model calibrated to North Carolina, we can assess multiple scenarios and parameters.
Methods: We developed a microsimulation model that simulates both opioid and synthetic use in North Carolina. Agents are generated using RTI's SynthPop™. Agents with an opioid use disorder may seek treatment during the simulation. The availability and success of this treatment are determined by input parameters linked to policy decisions. Transition probabilities for movement between opioid use states, synthetic use states, and treatment are calibrated using estimated totals for steady-state populations in each group. Additional information on the length of treatment and length of time to begin misusing opioids after treatment is also used. Opioid and synthetic-related overdoses are modeled and are calibrated to estimate annual overdose events and overdose deaths.
Results: By varying parameters for increased access to treatment, increased success rate of treatment, and lengthening the time it takes for individuals to begin using opioids again, total overdoses and overdose deaths both significantly drop. However, sensitivity analysis of model parameters (i.e., an agent's willingness to seek treatment, completion of treatment, etc.) shows that these parameters play a large role in model results. Model outcomes are determined by more than just making treatment available.
Conclusions: This simulation framework provides a quick method for testing the effect of policy decisions on treatment for opioid misuse in North Carolina. By exploring various parameter sets, the effect of decisions can be estimated for stakeholders.

W71. Developing a Core Outcomes Set (COS-OUD) for Opioid Use Disorder (OUD)-Related Research

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: As the National Drug Abuse Treatment Center for Clinical Trials Network (CCTN) continued to expand its portfolio of opioid studies, including those supported by the NIH's Helping to End Addiction Long-term (HEAL) initiative, the need for a core outcome set (COS) increased. A decision was made to develop a limited set of outcome measures that would be recommended for all OUD studies, which would allow comparison across studies.
Methods: Overseen by an expert workgroup, a modified, iterative, e-Delphi methodology was used to gain consensus among a specialist panel. Panel members included clinical practitioners and researchers in the field of OUD and staff from the Clinical Trials Network and their affiliated clinical and community sites. The panel members ranked 24 candidate items in four domains –disease status; behaviors, and functioning; treatment cascade; and morbidity and mortality – on a 9-point scale for importance. Ranking was done via

sequential rounds of anonymous, online questionnaires. A consensus threshold was achieved if at least 70% of the panel rated the measure as critical for inclusion in the COS-OUD.
Results: By expert consensus, a five-item core outcome set for opioid use disorder treatment efficacy and effectiveness research was developed. This followed four rounds of Delphi ranking by the panel members and a group discussion. The 5 outcomes selected were: (1) a single item global impression of improvement, (2) number of non-fatal overdose events, (3) at least two urine drug screening tests in past 21 days in different weeks negative for opioids, (4) number of days of continuous treatment, and (5) death from accidental or intentional ingestion of drugs.
Conclusions: The outcomes selected are critical to understanding important patient outcomes, are single or short items for documentation, and for self-report measures, less burdensome to patients.
Financial Support: NIH Grant UG1-DA049467

W72. Developing an Integrated Behavioral Treatment for Women With Opioid Use Disorder and Posttraumatic Stress Disorder: Patient and Provider Perspectives

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid use disorder (OUD) and posttraumatic stress disorder (PTSD) are significant public health concerns among women in the USA. In comparison to men, women show increasing rates of opioid overdose (640% among women vs. 478% among men), higher rates of severe trauma exposure, and a twofold risk of developing PTSD. Gender-specific treatments for women with OUD/PTSD are urgently needed to improve outcomes. Accordingly, the current ongoing pilot study interviewed women with OUD/PTSD and providers who work with this patient population about how to adapt an evidence-based, integrated behavioral treatment for substance use disorders and PTSD to address the gender- and opioid-specific needs of women with OUD/PTSD.
Methods: Women with OUD/PTSD (N=8) and providers (N=9) were interviewed for 60-90 minutes and completed a survey about their: (1) treatment experiences, (2) OUD and PTSD, and (3) treatment preferences. Data collection will be completed by March 2022 (target N = 30).
Results: All women with OUD/PTSD (87.5% white, 12.5% Black; Mean age = 43.0) identified as mothers and reported high PTSD symptoms (PTSD-Checklist 5: M=40.57, SD=25.09). The average age of OUD onset was M=28 (SD=10.53). Providers included 4 psychologists, 3 psychiatrists, and 2 master's level licensed counselors. Emerging themes among women include: (1) using opioids to cope with trauma-related physical and emotional pain; (2) preferences for integrated treatment delivered by group and individual therapy; and (3) desires to discuss life events that prompted opioid misuse in treatment. Among providers, emerging themes include: (1) inclusion of emotion regulation skills in treatment; (2) preference for shorter sessions; (3) interest in technology adjuncts; and (4) inclusion of therapeutic content on medication adherence.
Conclusions: Findings provide unique and important stakeholder perspectives on ways to modify the content and delivery of current integrated treatments to optimize outcomes for women with OUD and PTSD.
Financial Support: Office of Research on Women's Health and the National Institute on Child Health and Human Development (K12 HD055885; PI: McGinty)

W73. Effects of Adjunct Gabapentin on Treatment Outcomes During an Outpatient Buprenorphine Taper

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: Opioid dependence is a serious public health problem, particularly with the dramatic rise in prescription opioid (PO) abuse, but long-term opioid agonist maintenance with methadone or buprenorphine (BUP) may not be optimal for many PO abusers. We previously reported that gabapentin (GPP) reduced opioid use more than placebo (PLA) during a pilot clinical trial of GBP to improve 10-day BUP-assisted taper outcomes. We present data from the taper phase of a larger randomized, double-blind, placebo-controlled clinical trial examining the efficacy of GBP to improve outcomes in PO-dependent individuals undergoing outpatient BUP taper and transition to short-term depot naltrexone (NTX).
Methods: One hundred seventeen participants participated in an up to 12-week randomized, double-blind, placebo-controlled trial. During taper phase (weeks 1-3), participants attended clinic 5-6 days per week to receive study medications, attend weekly therapy, and complete assessments including craving, withdrawal and drug use. Participants were inducted onto 12 mg buprenorphine daily by day-2, week-1 and randomized to PLA or GBP (800 mg BID) starting day-3, week-1. A 10-day BUP taper started day-3, week-2 with doses of 1 mg on days 4/5 of week-3. Starting day-1 week-4, participants underwent assessments and began outpatient transition to depot NTX by day-5, week-4.
Results: Of 117 participants, 75 (64.1%) completed BUP detox. No baseline medication group differences in sex, race, age or study retention occurred. Preliminary analysis shows that craving and withdrawal measures decreased over time before increasing slightly at the end of the taper ($p<0.05$). Craving frequency significantly decreased from week 1 to week 2 for GBP subjects vs. PLA subjects ($p<0.05$). However, no significant medication group differences or medication group by time interactions otherwise occurred on craving, withdrawal, and opioid use.
Conclusions: Adjunct GBP did not appear to differentially improve treatment outcomes during the BUP taper.
Financial Support: This work is supported by NIDA grant R01DA036544-01A1 and authors have no disclosures.

W74. Examination of Sociodemographic Trends in Opioid Overdose Emergency Department Visits in Diverse Counties in New York State, 2010-2019

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: As with national trends, New York State has experienced marked increases in opioid-related overdoses (ODs) in recent years. To guide public health strategies, it is critical to assess how rates have varied across different demographic and geographic subgroups.
Methods: Patient information from hospital emergency department (ED) visits involving opioid-related poisoning diagnoses were obtained from the NY State Department of Health Statewide Planning and Research Cooperative System representing diverse NY counties (Erie, Onondaga, Monroe, and Kings/Brooklyn-NYC), 2010-2019. Zip-code-level poverty estimates (2011-2015) from the American Community Survey were linked to individual-level ED data to examine changes in opioid overdose ED visits over time and differences by sociodemographic characteristics.
Results: Like national trends, NY experienced exponential increases in opioid overdose ED visits between 2010-2019. Although White patients had higher rates of opioid OD as a proportion of ED visits than Black and Hispanic patients, the rate of increase was higher in Hispanic compared to Black or White patients, $p<0.001$. These findings persisted in each of the four counties except for Onondaga, where White patients experienced higher rates of increases in opioid OD compared to Black and Hispanic patients, $p<0.001$. Geographically, Brooklyn-NYC had lower opioid OD rates than upstate counties prior to 2016. However, after 2016, Brooklyn-NYC experienced the highest rate of increase of the four counties. There were also significant socioeconomic differences in opioid OD. Patients living in areas with more poverty experienced lower rates of opioid OD as compared to those in areas with less poverty, $p<0.001$. After 2018, this association reversed.

Conclusions: These findings highlight the importance of ongoing place-based epidemiological monitoring of socioeconomic, geographic, and racial-ethnic differences in opioid-related ED visits in NYS. Specifically, our findings call for prevention and treatment for opioid-related behavioral health conditions that incorporate individual and area-level social and economic conditions.

W75. Examining Gender Differences in the Relationship Between Social Bonds and Opioid Misuse Treatment Completion Among Justice-Involved Adolescents

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Drug Category Opiates/Opioids
Topic Criminal Justice
Abstract Detail Human
Abstract Category Original Research
Aim: Substance use disorder (SUD) and mass incarceration are two interrelated public health concerns facing adolescents in the United States. Unmet SUD treatment needs can be devastating for justice-involved adolescents (JIA), who are at greater risk of opioid use disorder (OUD) and overdose. Only a portion of adolescents who meet diagnostic criteria for OUD are referred for clinical diagnosis and complete treatment, and females may suffer harsher consequences of unmet treatment needs. Social bonds (i.e., connections to peers, family, and school) may also play an important role in treatment completion. However, a comprehensive study of the factors by which gender and social bonds impact opioid misuse (OM) treatment completion among JIA has not been conducted.
Methods: Stratified logistic regression analyses were employed to examine a statewide dataset of 79,570 JIA from the Florida Department of Juvenile Justice (FLDJJ). The FLDJJ sample consisted of JIA who were arrested and administered the Positive Achievement Change Tool (PACT) intake assessment between 2004-2015. Social bonds were operationalized by 14 PACT variables related to family, peer, and school attachments. Rates of treatment completion were obtained from the PACT and self-reported data.
Results: JIA with higher attachment scores had higher odds of OM treatment completion than those with lower scores, and these associations were stronger for females. Among females, family attachment was associated with a 45% increase, peer attachment was associated with an 86% increase, and school attachment was associated with a 72% increase in the odds of OM treatment completion compared to those without these attachments, respectively.
Conclusions: Results indicate the need for the development of gender-specific interventions to prevent and/or treat OM. OM treatment that incorporates and acknowledges the influence and protective nature of social bonds may be particularly effective among female JIA.
Financial Support: This research was supported by the University of Florida Substance Abuse Training Center in Public Health from the National Institute of Drug Abuse (NIDA) of the National Institutes of Health under award number T32DA035167 (PI: Dr. Linda Cottler). This research was also supported by the National Institute on Drug Abuse under award numbers 1K01DA052679 (PI: Dr. Micah Johnson), R25DA050735 (PI: Dr. Micah Johnson), and R25DA035163 (PI: Dr. Carmen Masson). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Florida Department of Juvenile Justice.

W76. Feasibility and Acceptability of Harm Reduction Vending Machines in Philadelphia

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Drug Category Opiates/Opioids
Topic Harm Reduction
Abstract Detail Human
Abstract Category Program Descriptions
Aim: Due in part to the opioid crisis, there was a 151% increase in HIV infections in persons who inject drugs (PWID) in Philadelphia. Harm reduction is an effective strategy to reduce HIV infection rates. Vending machines that contain harm reduction materials (VMHR) are a promising and innovative method

towards delivering critical supplies and information for PWID. Pilot evidence suggests VMHR are generally appropriate and feasible to PWID and staff at facilities that may house such vending machines.
We propose an exploratory, multi-stakeholder qualitative inquiry regarding the introduction of VMHRs in Philadelphia. The objective of this study is to understand the acceptability and feasibility of VMHR at a Federally Qualified Health Center (FQHC) and to understand potential barriers to its implementation. To date, there has not been a study that systematically examines factors that may impede or facilitate implementation of VMHR.
Methods (Optional): Interviewees will include individuals served by an FQHC (n = 15), FQHC clinical staff (n = 5), FQHC administrative leadership (n = 5), and members of surrounding community (n = 10). We will design a semi-structured interview based on hypothesized barriers to VMHR implementation, guided by the Consolidated Framework for Implementation Research. Topics will include the potential materials in VMHRs, community support, safety, legality, location, among others. We will use rapid qualitative techniques to analyze the interviews, which have been shown to provide valid findings in a short timeframe.
Conclusions: VMHR are an underutilized but potentially effective strategy towards reducing new HIV infections locally and nationally. The evidence and insights generated from our qualitative inquiry can be taken to scale at other FQHCs or other potential host sites in Philadelphia such as areas with high rates of injection drug use or substance use disorder treatment facilities.
Financial Support: Supported by a grant "Ending the HIV Epidemic": offered jointly by the University of Pennsylvania Leonard Davis Institute of Economics, the University of Pennsylvania Center for AIDS Research, and the Philadelphia Department of Public Health.

W77. HEALing Transitions: Training and Development of Opioid Use Disorder (OUD) Linkage and Retention Nurse/Social Work Care Navigator Programs

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Program Descriptions
Aim: “HEALing Transitions” are novel nursing and social work care navigation programs designed as part of the Healing Communities Study (HCS) to deliver client-centered, evidence-based care to individuals with opioid use disorder (OUD). The aim of the Linkage program is to connect individuals with OUD to medication for opioid use disorder (MOUD) treatment and follow until care is established. The aim of the Retention program is to facilitate retention in MOUD treatment by proactively addressing client barriers and providing additional support. The goal of this presentation is to provide details regarding the development and training of these programs.
Methods (Optional): HEALing Transitions was developed by integrating evidence-based best practices from HIV care navigation models with the HCS Opioid-Overdose Reduction Continuum of Care (ORCCA) approach. Training consists of approximately 55 hours across seven domains: administrative onboarding, standard medical care navigation, substance use disorder and MOUD education, OUD-specific care navigation, client assessment, linkage and retention program implementation, and opioid-overdose education and naloxone distribution (OEND).
Results (Optional): To date, 19 care navigators have been trained and deployed across 27 community agencies (e.g., office-based opioid treatment, opioid treatment programs, and detention centers). A total of 170 clients (22 Linkage and 148 Retention) have enrolled. Of the 22 linkage clients, 17 (77.3%) are active in linkage services or have successfully transitioned to MOUD maintenance. Of the 148 retention clients, 115 (77.7%) have been retained in MOUD treatment. Qualitative data from care navigator reports indicate trainings specific to MOUD education, OUD care navigation, and risk reduction have been particularly beneficial in successfully working with clients.
Conclusions: The HEALing Transitions programs provide an evidence-based approach to OUD care navigation. Initial data indicate that navigators have successfully engaged clients, linked to MOUD, and provided OEND and retention services. Further research will evaluate the effectiveness of these programs on retention and opioid overdose death reduction.

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W78. Houselessness and Treatment Outcomes Among Black Adults With Opioid Use Disorder: A Secondary Analysis of X:BOT

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Drug Category Opiates/Opioids
Topic Racial/Ethnic Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Black individuals and people experiencing houselessness (PEH) are both heavily impacted by the opioid epidemic. We sought to identify the sociodemographic and clinical characteristics associated with houselessness, and explore the relationship between houselessness and treatment outcomes among Black individuals.
Methods: This is a secondary analysis of the subgroup of Black participants (n=73) enrolled in "X:BOT," a 24-week multisite randomized clinical trial comparing the effectiveness of extended-release naltrexone vs. sublingual buprenorphine-naloxone (n=570). Participants were considered houseless if at baseline they answered "yes" to the question "are you currently homeless or living in a shelter?" as a part of a quality of life questionnaire. Outcomes included: medication initiation, return to use of opioids assessed by both self-report and urine toxicology, and medications for opioid use disorder (MOUD) engagement at 28 weeks post-randomization. Descriptive statistics were performed.
Results: Black participants were mostly male, age 21-30, and unmarried. Among PEH, more were uninsured (45.5% [10/22] vs. 19.6% [10/51]), unemployed (77.3% [17/22] vs. 64.7% [33/51]), and reported alcohol (40.9% [9/22] vs. 23.5% [12/51]) and sedative intoxication (54.5% [12/22] vs. 17.6% [9/51]) within the previous 30 days. Compared to housed individuals, a slightly higher proportion of PEH had successful study initiation onto study medication (81.1% [18/22] vs. 72.6% [37/51]), but similar proportions of return to use (68.2% [15/22] vs. 68.6% [35/51]) and MOUD engagement at 28 weeks of participants who participated in follow up (72.2% [13/18] vs. 69.7% [23/33]).
Conclusions: In this exploratory study, we observed slightly higher levels of study medication initiation, but similar levels of return to use and MOUD engagement at 28 weeks among Black PEH. The results suggest that efficacious medication-based treatment of OUD among PEH is possible with clinical and psychosocial support. Strategies are needed to further enhance OUD treatment outcomes among PEH with OUD.

W79. Incubation of Conditioned Opioid Withdrawal Avoidance in Methadone-Dependent Male and Female Rats

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Responding to cues paired with positive reinforcing effects of opioid drugs progressively increases (incubates) during abstinence in rats. We adapted a primate opioid negative reinforcement model (Downs and Woods. Pharmacol Rev. 1975) to study whether responding to withdrawal-paired cues incubates during abstinence.

Methods: We trained rats (n=40; 20F) to lever-press for food and to escape from mild-footshock for 21 days. Next, we catheterized them and implanted methadone (10 mg/kg/day)-containing minipumps to induce opioid dependence. We then paired non-contingent naloxone (20 μg/kg/infusion) with a compound light+tone cue 4 times (single session). Next, we trained the rats to avoid naloxone (1 μg/kg/infusion) injections for 8 sessions (30 trials/session). During the trials, the rats were exposed to the withdrawal cue for 20 s before naloxone injections and could avoid the injections by lever pressing. Next, we determined within-session naloxone-avoidance dose-response (0.32-to-10 μg/kg/infusion). Finally, we tested the rats for conditioned avoidance responding to the withdrawal cue under extinction conditions 1 and 15 days after minipump removal (incubation tests).
Results: The rats learned to lever press for food pellets and to avoid mild footshock. They also learned to lever press to avoid naloxone-induced withdrawal and decreased their lever pressing for both food and naloxone avoidance with increasing naloxone doses. Most important, during incubation testing, lever presses to avoid the naloxone-paired cue were higher after 15 abstinence days than after 1 day. This incubation effect was stronger in females.
Conclusions: We adapted a negative reinforcement primate model to rats and showed that conditioned opioid withdrawal avoidance responding incubates during abstinence.
Financial Support: NIH/NIDA

W80. Monovalent and Bivalent Vaccination Strategies to Protect Against Deliberate and Accidental Exposure to Carfentanil and Mixtures of Carfentanil and Fentanyl in Rats

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Animal Study
Abstract Category Original Research
Aim: The incidence of drug-related fatal overdoses has significantly increased in the last decade due to the widespread availability of illicit fentanyl and other potent synthetic opioids such as carfentanil. Deliberate or accidental consumption or exposure to fentanyl and carfentanil induce respiratory depression and bradycardia that can be difficult to reverse by the opioid receptor antagonist naloxone. Vaccines offer a promising strategy to reduce the incidence of fentanyl- and carfentanil-related fatalities. This study reports the development of monovalent and bivalent vaccination strategies that elicit polyclonal antibody responses effective in protecting against the pharmacological actions of carfentanil, fentanyl, or carfentanil/fentanyl mixtures.
Methods: This study reports the development of monovalent and bivalent vaccination strategies that elicit polyclonal antibody responses effective in protecting against the pharmacological actions of carfentanil, fentanyl, or carfentanil/fentanyl mixtures. Male rats (n=6/group) were vaccinated with conjugates containing either individual fentanyl- or carfentanil-based haptens, or their combination in bivalent formulations. Rats were subsequently challenged with carfentanil, fentanyl, or their combination.
Results: A lead vaccine was protective against carfentanil-induced antinociception, respiratory depression, and bradycardia. Efficacy against both fentanyl and carfentanil was achieved by combining lead anti-carfentanil and anti-fentanyl vaccines through either a heterologous prime/boost or a co-administration bivalent vaccination strategy.
Conclusions: These preclinical data support the development of vaccines as a viable strategy to counteract toxicity and overdose from carfentanil, fentanyl, or their mixtures.
Financial Support: This work was supported by the National Institute on Drug Abuse (NIDA) and the National Institute of Neurological Disorders and Stroke (NINDS) under award number UG3DA04838602 (MP), T32DA007097 (MMW and BC), F31DA054760 (BC) and the University of Minnesota Graduate Program in Pharmacology (DS).

W81. Open Label Trial of Lofexidine-Assisted Non-Opioid Induction Onto Naltrexone Extended-Release Injection for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Opioid use disorder (OUD) is a major public health problem and innovative medication strategies are needed. The extended-release injectable formulation of naltrexone (ER-NTX), an opioid receptor antagonist, is an effective treatment for OUD, but the need for an opioid-free period during the induction phase of treatment is a barrier to treatment success, particularly in the outpatient setting. For fentanyl-using patients, buprenorphine treatment during an ER-NTX induction is potentially more complicated and non-opioid options are desirable.
Methods: In an open-label, uncontrolled 10-week outpatient clinical trial to evaluate the feasibility, safety and tolerability of using lofexidine, an alpha-2-adrenergic agonist, to facilitate induction onto naltrexone for extended-release injectable suspension in 20 adults with OUD. Participants were scheduled to receive two monthly ER-NTX injections (380 mg). The COVID-19 pandemic resulted in a modification of the study methods after enrolling 10 participants. The second group of 10 participants attended most of the induction period visits remotely.
Results: Ten (50%) of enrolled participants received the first ER-NTX injection. All heroin users (n = 14) were fentanyl-positive, and all prescription painkiller users (n = 6) were fentanyl-negative. Rates of induction success did not differ by the presence of fentanyl (fentanyl-positive 57.1%; fentanyl-negative 33.3%) or remote visit attendance (in-person 60.0%; hybrid remote 40.0%), although the small sample size provided limited statistical power.
Conclusions: This study provides preliminary evidence supporting the feasibility of inducting patients with OUD onto ER-NTX using lofexidine, including patients using fentanyl.
Financial Support: US World Meds

W82. Opioid Use Disorder (OUD) and Treatment for Opioid Problems Among OUD Symptom Subtypes

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Drug Category Opiates/Opioids
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: Although it is well established that most individuals with opioid use disorder (OUD) do not receive treatment, it is important to understand heterogeneity of OUD symptoms in the US population and whether OUD diagnosis or receipt of treatment differs by symptom subtypes.
Methods: A sample of respondents (n=10928) reporting past-year abuse/misuse of heroin or prescription opioids was drawn from the 2015-2018 National Survey on Drug Use and Health (NSDUH). Latent class analysis (LCA) was used to identify classes (subgroups) based on patterns of OUD symptoms (DSM-IV abuse and dependence). The probability of OUD and treatment in the past year for opioid-related problems were estimated for each class.
Results: A 5-class model provided the best fit. A SEVERE class with nearly all OUD symptoms included 6% of the sample. Intermediate symptom classes included: TOLERANCE (15%), characterized by presence of only tolerance symptoms; DEPENDENCE (6%), characterized by DSM-IV dependence symptoms but not abuse; and WORK/LIFE (3%), characterized by giving up important activities and using opioids despite problems. The remainder of the sample (71%) was in the LOW class with ≤1 OUD symptom. Although nearly all of those in the SEVERE, DEPENDENCE, and WORK/LIFE classes met criteria for OUD (98-100%) they differed in receipt of past-year treatment for opioid problems (46%, 24%, 18%, respectively). One-third (35%) of the TOLERANCE class had an OUD diagnosis and 7% received opioid treatment. No one in the LOW class had an OUD diagnosis and 2% received opioid treatment.
Conclusions: There were considerable quantitative and qualitative differences in patterns of OUD symptoms and receipt of treatment among those who misused opioids, particularly among those with OUD.

The findings indicate substantial unmet need for OUD treatment, even among those with nearly all OUD symptoms, and point to patterns of heterogeneity within OUD that can inform development of individualized treatment programs.
Financial Support: This research was supported by Indivior, Inc.

W83. Overdose Fatalities in Maryland Jurisdictions and Implementation of Overdose Prevention Strategies

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: This study aimed to summarize implementation of overdose prevention and response programs in all 24 counties in Maryland, and to identify whether counties with high opioid overdose death rates in 2019 were more likely to implement a greater number of programs by 2021.
Methods: Data on program implementation were from Maryland's Opioid Operational Command Center (OOCC), which supports state and local efforts to respond to the overdose crisis. OOCC's Program Inventory describes implementation of 145 programs across 12 sectors (e.g., public health, education, judiciary) and 10 cross-cutting programs designed to broaden access to naloxone. Implementation of each program was classified as substantial, partial, planned, or none. We used non-parametric tests to estimate associations between 2019 overdose death rates and substantial implementation (SI) of programs by 2021, at the county level. We examined: [a] all 145 programs, [b] programs within each of the 12 sectors, and [c] the 10 naloxone programs.
Results: The median percentage of SI was 51% for all 145 programs and 70% for naloxone programs. The social services sector had the highest median percentage of SI across counties (80%), whereas higher education had the lowest (25%). The association between overdose mortality and overall SI across all 145 programs was not statistically significant. There was a significant association between overdose mortality and SI of public health programs (e.g., fentanyl test strips; p=0.04), but not for programs in the other 11 sectors.
Conclusions: We did not find evidence that high overdose death rates in 2019 spurred program implementation by 2021. The emergence of the COVID-19 pandemic in 2020 may have limited progress in program implementation. Seven of the state's 24 counties had overdose mortality rates above the state median (i.e., >30 per 100,000) but had noteworthy gaps in implementation. These counties may require additional support (e.g., funding, training) to increase program uptake.
Financial Support: Cooperative Agreement number 6NU17CE924961 from the Centers for Disease Control and Prevention (CDC)

W84. Pain in Recovery From Opioid Use Disorder: The Importance of Acute and Chronic Pain

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The causal role of chronic pain in initiation of opioid use disorder (OUD) has been well characterized, but limited information exists regarding how pain affects OUD recovery. Moreover, potential differences in OUD recovery outcomes between chronic and acute pain remain poorly understood.
Methods: This investigation included a sample of n = 214 individuals who participated in the RECOVER-LT study (NCT04577144), a single 5-year follow-up assessment of individuals in recovery from OUD.

Measures collected included demographics, pain duration and severity, substance use, quality of life, opioid dependence, and substance use disorder treatment utilization. t-test, chi-squared test, and analysis of variance (ANOVA) were utilized for comparisons.
Results: Of the 214 participants in this cross-sectional study, 74% reported chronic pain, 16% reported acute pain, and 10% reported no pain. No significant differences in demographics were observed among pain groups (ps>0.05). Acute pain, similar to chronic pain, showed significantly higher proportions of opioid, heroin, and tobacco use in the past 30 days (p=0.009, p=0.010, p=0.005, respectively) compared to the no pain group, but no significant differences in cannabis use were observed among pain groups (p=0.129). No significant differences in opioid dependence (p=0.055) or treatment utilization (p=0.581) were observed among pain groups. Both the acute and chronic pain groups exhibited significantly worse depression (p=0.002), life stress (p=0.002), psychological distress (p=0.001), Treatment Effectiveness Assessment health (p<0.001), and quality of life (ps<0.036).
Conclusions: Individuals with acute pain and chronic pain reported higher rates of recent use across several substances relative to the no pain group. Additionally, both pain groups exhibited poorer physical health, mental health, and quality of life. These results highlight the importance of pain assessment and management in OUD recovery.
Financial Support: This work was supported by Indivior, Inc., North Chesterfield, VA, USA.

W85. Preclinical Profiling of the Ampakine HJC0122 as a Novel Therapeutic for Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Behavior
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Opioid use disorder (OUD) produces long-term effects on neurocircuitry and synaptic plasticity which can lead to unique patterns of gene expression, possibly contributing to long-term neuroadaptations. α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) regulation is synonymous with synaptic plasticity and linked to neuroadaptations associated with chronic opioid use. AMPARs also regulate functional processes underlying opioid-mediated behaviors, including antinociception and respiratory rhythmogenesis. AMPAR positive allosteric modulators (PAMs), (i.e. AMPAkines) potentiate AMPAR function and reduce pain hypersensitivity in rodents and attenuate opioid-induced respiratory depression without loss of analgesia in humans. We tested the hypothesis that our novel, highly potent AMPAkine HJC0122 will demonstrate a promising preclinical profile as an OUD therapeutic.
Methods: Male Sprague-Dawley rats (n=24) were trained to self-administer fentanyl (0.001 mg/kg/inf). Once stable, rats were treated with HJC0122 (0, 20, 30 mg/kg, i.p.) 20 min prior to a fentanyl self-administration session to ascertain efficacy to suppress fentanyl intake. Additional rats were tested on the incremental hot plate assay to assess thermal sensitivity following HJC0122 (0, 20 mg/kg i.p.) alone or in combination with fentanyl (0, 30 μg/kg, s.c.) (n=59). Lastly, a naïve group of rats was treated with HJC0122 (0, 20 mg/kg i.p.) followed by escalating doses of fentanyl (12.5, 12.5, 25, 50 μg/kg s.c.) to profile effects on physiological parameters (arterial oxygen saturation, heart rate, pulse distension) assessed with pulse oximetry (n=48).
Results: Notably, HJC0122 suppressed fentanyl self-administration without evidence of impairment of other measures. HJC0122 also potentiated fentanyl-induced antinociception, but did not alter fentanyl-induced decreases in oxygen saturation, heart rate or pulse distension.
Conclusions: These data suggest that HJC0122 exhibits the preclinical profile of a compound that may suppress opioid intake with a limited side effect profile. We are actively exploring the molecular mechanisms through which HJC0122 suppresses opioid intake, with the goal to develop HJC0122 as a therapeutic compound for OUD.
Financial Support: U18 DA05245 (NCA, KAC, JZ); R00 DA03374 (NCA); TL1 TR001440 (AES)

W86. Retail Pharmacy Naloxone Distribution and Overdose Mortality in Rhode Island, Massachusetts, and New York City, 2016-2018

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: Naloxone is an effective antidote for opioid overdose; naloxone distributed to people at high risk for overdose has been associated with reduced overdose death rates, however, associations of retail pharmacy-distributed naloxone with overdose mortality have not been evaluated. We aimed to assess the independent association of pharmacy and community-based naloxone distribution with fatal opioid overdose rates.
Methods: Our analytic cohort uses retail pharmacy claims data from Symphony Health, community distribution data from health departments in Massachusetts, Rhode Island, and New York City, opioid overdose data from the National Center for Health Statistics, and publicly available American Community Survey data. Data were analyzed by 3-digit ZIP Code and calendar quarter-year (2016Q1-2018Q4), and observations were weighted by population. We regressed opioid-related mortality on retail-pharmacy and community naloxone distribution, and community-level demographics using a linear model with ZIP Code fixed effects and a time trend. Both types of naloxone distribution were parameterized using a level effect (current-quarter distribution), and a change effect (change in distribution from prior to current quarter).
Results: The unadjusted naloxone distribution rate more than doubled from 97 kits per 100,000 persons in Q1–2016 to 257 kits per 100,000 persons in Q4–2018 while the unadjusted opioid overdose mortality rate fell from 8.1 per 100,000 persons to 7.2 per 100,000 persons. We found that the level of naloxone distribution (both pharmacy and community) was positively and significantly associated with fatal opioid overdose rates, but did not detect associations between overdose mortality and the change in pharmacy or community naloxone distribution rates
Conclusions: Across NYC, RI, and MA pharmacy and community naloxone distribution was correlated with fatal overdose, getting to communities where it was needed most. Yet, in the midst of high rates of overdose driven by fentanyl in the drug supply, naloxone distribution alone was not enough to reverse the opioid-overdose crisis.
Financial Support: National Institutes of Health (grant numbers R01DA047408, P30DA040500, R01DA046527, and R01CE002999)

W87. Self-Management Strategies and Utilization of Medications for Opioid Use Disorder: A Qualitative Systematic Review

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Theoretical/Commentary
Aim: This will be a theoretical study of patient self-management (PSM) strategies in opioid use disorder (OUD) outpatient treatment programs (OTP)s utilizing methadone and buprenorphine. Of particular interest is the impact on retention and patient self-efficacy in OTPs after introducing these strategies. This study's goals will be to systematically evaluate qualitative research studies to better understand the clinically appropriate definition of and elaborate on the implementation of specific PSM strategies.
Conclusions: This study demonstrates that the implementation of PSM strategies in OTPS offering methadone and buprenorphine to patients diagnosed with OUD results in improve patient retention in treatment, improved patient self-efficacy, and improved clinical outcomes.

W88. Sleep Architecture of OUD Patients: A Comparison of Watchpat 300 and NPSG

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Drug Category Opiates/Opioids
Topic Other
Abstract Detail Human
Abstract Category Original Research
Aim: Patients with Opioid Use Disorder (OUD) often experience suppressed slow-wave and REM sleep, which is associated with a higher likelihood of relapse. The WatchPAT™300 (WP300) device is a home-care diagnostic that detects sleep disorders and sleep staging. It is a wrist-worn actigraph with a finger-oximeter probe. The aim of this on-going research is to compare WP300 sleep staging to the gold standard Nocturnal Polysomnogram (NPSG) in OUD patients.
Methods: After completing a two-week OUD detoxification regimen at an inpatient SUD facility, sleep (8-hr) is being recorded (using both NPSG and WP300) on the final night of treatment after receiving suvorexant (10, 20mg) or placebo at bedtime.
Results: In two completed patients results show in patient A, total sleep time (TST) of 450.5 mins in the NPSG; light sleep (stages N1+N2) accounted for 77.90% (351 mins), deep sleep (stage N3) 8.3% (37.5 mins) and REM 13.80% (62 mins). WP300 showed a TST of 432 mins; light sleep accounted for 67.8% (292.9 mins), deep sleep 9.7% (41.9 mins) and REM 22.5% (97.2 mins). Patient B's NPSG results show TST of 403.6 mins, of which light sleep accounted for 73.4% (296.1 mins), deep sleep 2.5% (10 mins) and REM 24.2% (97.5 mins). In comparison, patient B's WP300 report displays TST of 421 mins, of which light sleep accounted for 64.4% (271.1 mins), deep sleep 16.2% (68.2 mins) and REM 19.5% (82.1 mins).
Conclusions: In comparison to NPSG, the WP300 initially appears less sensitive when distinguishing light sleep from deep sleep and wake vs REM sleep. While more evidence will be collected, a diagnostic device that differentiates between slow-wave non-REM sleep and REM sleep may be useful in assessing at-home sleep in OUD patients.
Financial Support: National Heart, Lung, and Blood Institute 1U01HL150551 awarded to Mark K. Greenwald, Ph.D. and Timothy A. Roehrs, Ph.D.

W89. Telehealth Visits Support Buprenorphine Induction During the Covid-19 Pandemic

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Drug Category Opiates/Opioids
Topic Policy
Abstract Detail Human
Abstract Category Original Research
Aim: Regulatory changes implemented under the COVID-19 Public Health Emergency allowed initiation of transmucosal buprenorphine medication for opioid use disorder (bup MOUD) via telemedicine, effective March 16, 2020. This study evaluated the uptake of bup MOUD in 2020 among a commercially insured population.
Methods: Using the IBM MarketScan commercial claims database, we examined a subset of 22,161 patients that 1) had any bup MOUD fills in 2020, 2) were aged 18-64 in 2020, and 3) had 14 months of continuous enrollment (Nov-2019 to Dec-2020). A 60-day lookback identified treatment inductions. Telehealth claims were identified with CMS and AAFP definitions (procedure, place of service, or modifier). We considered a bup MOUD fill telehealth-associated if there was a telehealth claim including an OUD diagnosis code for service 0-7 days prior to the fill. We examined bup MOUD patients with at least one telehealth-associated fill, and treatment inductions with a telehealth-associated first fill.
Results: The number of bup MOUD patients increased from 18,043 in Q1-2020 to 18,922 in Q4-2020. The proportion of patients with at least 1 telehealth-associated bup MOUD fill also changed across the quarters ($X2 = 1,855$, $p < 0.001$), from 3.5% in Q1-2020 to 14.2% in Q4-2020, peaking at 17.5% (3,197) in Q2-2020. In contrast to the increasing number of patients overall, bup MOUD inductions decreased from 2,274 in Q1-2020 to 2,023 in Q4-2020, bottoming out at 1,938 in Q2-2020 ($X2=32.2$, $p<0.001$).The proportion of patients with telehealth-associated induction fills increased from 1.0% during the tele-induction policy transition period in Q1-2020 to 9.8% (190) in Q2-2020 ($X2=166.6$, $p<0.001$) and did not change significantly during Q2-Q4, 2020 ($X2=5.04$, $p=0.08$).

Conclusions: Telemedicine regulatory changes implemented under the COVID-19 Public Health Emergency supported access to maintenance and initiation of transmucosal buprenorphine.
Financial Support: UL1TR001998, UM1DA049406

W90. The Heroin Hug: Opioids Acutely Produce Feelings of Being Secure and Loved

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Human
Abstract Category Original Research
Aim: The Brain Opioid Theory of Social Attachment provides evidence that the endogenous opioid system is critical for forming and maintaining social bonds. We sought to assess whether reported acute subjective effects of opioids are associated with positive social feelings relative to other substances.
Methods: We recruited participants (n = 254) using Prolific, an online data collection platform. We used a novel measure to assess experiences of being high among people with histories of problematic substance use whose primary drug was alcohol, marijuana, methamphetamine, or opioids across four categories of feelings: positive (social/nonsocial) and negative (social/nonsocial). We used ANOVA to determine if there was a relationship between drug of choice and feeling endorsement. We used logistic regression to determine which specific items were associated with opioid use.
Results: Reported (retrospective) acute opioid effects during initial use included higher levels of positive social feelings than other drugs ($df = 3$, $F = 3.10$, $p < 0.05$). There was no significant difference in the other three feeling categories. A step-wise binary logistic regression was carried out to determine which positive feeling items were differentially associated with opioids (relative to other drugs). In the initial use period, the items 'like a hug' (standardized B = .44) and 'secure' (standardized B = .31) passed the significance threshold (a = .05) for retainment in the model as positive predictors. The item 'excited' was retained as a negative predictor (B = .46). We repeated this analysis with the experience during later problematic use; only the 'like a hug' item was differentially linked with opioid use (B = .51).
Conclusions: These findings indicate that the "heroin hug" may be a common experience. This has clinical implications: social supports may be a high-impact therapeutic target for those with a history of opioid use.
Financial Support: Funding was awarded from the USC Department of Psychology.

W91. The Path Home Trial: A Comparative Effectiveness Study of Optimal Intervention Strategies for Perinatal Opioid Use Disorder in Rural Kentucky

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Drug Category Opiates/Opioids
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Appalachian Kentucky is especially impacted by high rates of perinatal opioid use disorder (OUD). Although medication for OUD (MOUD) during pregnancy improves maternal and neonatal outcomes, knowledge of the best method of delivery of prenatal MOUD in rural settings is lacking. PATHways, a UK based clinic, integrates prenatal care with counseling and MOUD. The PATHhome study extends this model to underserved communities in Kentucky through a comparative effectiveness trial using individual telehealth sessions versus group sessions to provide a standardized OUD-pregnancy specific education/counseling curriculum.
Methods: PATHhome is a randomized cluster trial comparing two intervention arms across 11 sites. This presentation examines intervention participation, defined as session attendance at telemedicine or group out of possible sessions available, as one of the priority study outcomes. Beginning March 2019, 165 pregnant women have been enrolled from community sites. Eligibility criteria include: gestational age 6-32 weeks; diagnosed OUD; current MOUD treatment. Intervention occurs every 2 weeks and major data collection occurs at enrollment, 28-32 weeks, delivery, and 3- and 6-months post-partum.

Results: Participants' mean age is 29.3 years and mean gestational age is 19 weeks. 69 (41.6%) receive MOUD from their OB provider in an integrated model; 67(40.4%) started MOUD in pregnancy. 84 (50.6%) take Subutex; 56(33.7%) Suboxone; 9 (5.4%) methadone. 34 (20.5%) report an overdose history and 73 (44.0%) are HCV+. In terms of social history, 95 (57.2%) reside with baby's father; 129 (77.7%) expect father to be involved in baby's life. Patients report significant depression scores at intake – mean is 10.86. Thus far, 69 (41.6%) have delivered. Preliminary data suggest that patient engagement in the group arm may exceed telehealth ($p<.05$ in interim analysis).
Conclusions: This study will contribute to the evidence base on approaches to establish integrated prenatal care and access to MOUD in real world regional healthcare practices.
Financial Support: This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Project Program Award (MAT-2017C2-7842). All statements in this report, including its findings and conclusions, are solely those of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute (PCORI), its Board of Governors or Methodology Committee.

W92. The Relationship Between Resilience Phenotypes and Psychological Functioning in Individuals With Opioid Use Disorder

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Drug Category Opiates/Opioids
Topic Mechanisms of Action
Abstract Detail Human
Abstract Category Original Research
Aim: Resilience is a multidimensional psychobiological trait characterized by the maintenance of homeostatic functioning in response to stress and adverse experiences. A previous investigation among opioid use disorder (OUD) patients identified two resilience phenotypes (High and Low) using Connor-Davidson-Resilience-Scale-25 (CD-RISC-25)] and Revised-NEO-Personality-Inventory (NEO-PI-R). The present study aimed to examine the relationship between these previously identified resilience clusters and psychological symptoms within a sample of individuals with OUD.
Methods: Data were obtained from an ongoing investigation examining the effects of heroin use on epigenetic aging among individuals of African ancestry. Participants met DSM-5 criteria for OUD, while severe psychiatric disorders were exclusionary. Participants completed several measures to assess their current and history of drug use, psychological functioning [Beck Depression Inventory-II (BDI-II), range: 0-63; Perceived Stress Scale (PSS), range: 0 to 40; State-Trait Anxiety Inventory (STAI), range: 20 to 80]. Multivariate analysis of covariance (MANOVA) compared resilience clusters regarding psychological symptoms (depression, anxiety, and stress).
Results: Sixty-seven participants [17.9% female; mean age 48.5 (±6.84) years] were included in the current analysis. The mean duration of opioid use was 18.5 (±10.7) years. The MANOVA revealed statistically significant differences between groups [$\Lambda = 0.726$, $F(3, 56) = 7.05$, $p < .001$]. Univariate F-tests indicated that the "High resilience cluster" had significantly lower PSS, $F(58,1) = 11.49$, $p <0.001$, BDI-II, $F(58,1) = 6.66$, $p < 0.01$, and STAI scores, $F(58,1) = 21.17$, $p < 0.001$.
Conclusions: Our findings suggest the phenotype characterized by "High" resilience is associated with improved psychological functioning among individuals with OUD. Future studies should explore the malleability and behavioral underpinnings of these resilience phenotypes
Financial Support: NIDA grant R21DA043199 to Dr. Jermaine Jones

W93. Trends in Opioid and Stimulant Treatment Admissions and Overdose Mortality in American Rural and Urban Areas

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Drug Category Opiates/Opioids
Topic Treatment
Abstract Detail Human
Abstract Category Original Research

Aim: This study examined trends of treatment admissions (primary drug being opioids or stimulants) and associated overdose mortality in 2017 to 2019 across American rural and urban areas.
Methods: We combined 2017-2019 Treatment Episode Data Set (TEDS) Admissions and CDC opioid and stimulant overdose mortality data. Based on patients' recorded Core Based Statistical Area (CBSA) in TEDS, we defined urban as having CBSA designation codes and rural as the absence of a CBSA code. In addition, we used Health Resources and Services Administration (HRSA) rural list to define rural counties. Mixed effects models were used to examine associations between treatment admissions and overdose mortality over time in rural versus urban areas.
Results: Rural and urban areas have different trends in treatment admissions for opioid and stimulant use disorders; rural areas showed an overall increase from 2017-2018 followed by a decrease in 2019, while urban showed a continued decrease over the 3 years. Overdose mortality for both opioids and stimulants were lower in rural than urban areas ($p<0.001$), but all increased in 2019 after a decrease in 2018 relative to 2017. In urban areas, higher mortality was associated with lower treatment admissions for both opioids (-0.0269, $p<0.001$) and stimulants (-0.0197, $p<0.001$). However, the associations between mortality and admissions were not significant for rural areas.
Conclusions: The observation of lower overdose mortality associated with higher numbers of treatment admissions (although only significant for the urban counties) highlights the importance of treatment. The decreasing numbers of treatment admissions for opioid and stimulants for both rural and urban counties is of concern particularly in the context of the COVID pandemic that has worsened substance use disorders and overdose mortality.
Financial Support: This study was funded by National Institute on Drug Abuse (NIDA) UG1DA049435

W94. Two Novel Classes of Opioid Analogs: Discriminative Stimulus and Antinociceptive Effects

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Abstract Detail Animal Study
Abstract Category Original Research
Aim: Analogs of two older opioid compounds, etonitazene and bucinnazine (AP-237) have recently been seen in the illicit drug market, some of which are quite potent and have led to increases in overdoses. The morphine-like interoceptive and antinociceptive effects of three "nitazene" (2-benzylbenzimidazole) analogs and four AP-237 (piperazine-amide) analogs were tested.
Methods: The discriminative stimulus effects of morphine, fentanyl, etonitazine, butonitazene, clonitazene, AP-237 (bucinnazine), 2-methyl-AP-237, para-methyl AP-237 and AP-238 were tested in male Sprague-Dawley rats trained to discriminate morphine from saline. Antinociception was tested using a warm-water tail-flick assay (50° C) in male Swiss-Webster mice.
Results: para-Methyl AP-237 failed to produce significant levels of morphine-appropriate responding. The remaining test compounds, morphine, fentanyl, etonitazine, butonitazene and clonitazene, AP-237, 2-methyl-AP-237, and AP-238 fully substituted for the discriminative stimulus effects of morphine. Naltrexone blocked the discriminative stimulus effects. All of the synthetic opioids, etonitazine, butonitazene, clonitazene, AP-237, 2-methyl-AP-237, para-methyl AP-237 and AP-23 produced full antinociceptive effects at 50° C, as did morphine and fentanyl. There was a wide range in the time courses of the test compounds, ranging from 90 to 180 min. Naltrexone blocked the antinociceptive effects.
Conclusions: All of the analogs, both the nitazenes and piperazine-amides produced opioid-like antinociceptive effects blocked by naltrexone, which supports an opioid mechanism. Most of the analogs produced morphine-like interoceptive effects that were blocked by naltrexone and therefore have the potential to be used recreationally as substitutes for legal and illegal opioids. para-Methyl AP-237 did not produce morphine-like interoceptive effects, and may not be well accepted by users seeking a high. Etonitazene, as previously reported, was more potent than fentanyl, so may have increased risk for overdose. The remaining compounds mostly had potencies closer to morphine than fentanyl, so may not have as high a risk for overdose.
Financial Support: Supported by DEA contract DOJ 15DDHQ21F00000340.

W95. What is Success in Treatment for Opioid Use Disorder? Perspectives of Physicians and Patients in Primary Care Settings

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: Clinicians and researchers have traditionally relied on treatment retention and opioid abstinence as the primary measures of treatment success for people with opioid use disorder (OUD). However, these measures may not capture the range of clinically important treatment outcomes. The study sought to identify indicators of success in primary care-based medication for OUD (MOUD) treatment from the perspectives of patients with OUD and the physicians who treat them.
Methods: Patients (N = 18; M age = 38.1 years, SD = 11.5; 44% female) and physicians (N = 14; M age = 34.6, SD = 6.8 years; 57% female) were recruited from two academic family medicine residency clinics in the Upper Midwest to participate in semi-structured qualitative interviews. Participants reflected on signs of progress and success in primary care MOUD treatment. Interviews were recorded, transcribed, and analyzed using an inductive thematic analysis approach.
Results: Seven themes of success emerged: (1) staying sober; (2) tapering off buprenorphine; (3) taking steps to improve physical and mental health; (4) improved psychological well-being; (5) improved relationships; (6) improved role functioning; and (7) shift in identity (decreased shame). Interviews with both patients and physicians supported five of the seven themes, with patients also describing themes of tapering off buprenorphine and a shift in identity.
Conclusions: Themes suggest that a wider view of success, in addition to maintaining sobriety, is needed when considering outcomes for MOUD programs delivered in primary care settings. Future work to identify appropriate outcome measures and potential adjunctive treatments is needed.
Financial Support: This work was supported by the Substance Abuse and Mental Health Services Administration (SAMHSA) State Opioid Response Grant through the Minnesota Department of Human Services (H79TI080248) to RL. These sponsors had no role in the study design, collection, analysis, or interpretation of the data and presentation of findings.

W96. "I Feel Like I'm Floating in Limbo": Understanding the Impacts of the COVID-19 Pandemic on Persons Who Use Illicit Opioids in Arizona

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research
Aim: The overdose crisis in the U.S. has escalated further since the start of the COVID-19 pandemic. The purpose of this study is to characterize the impacts of the COVID-19 pandemic on drug use experiences among persons who use illicit opioids (PWUO) in Arizona.
Methods: Between 12/2020 and 06/2021, in-depth qualitative interviews were conducted with 22 PWUO from across Arizona. Participants were recruited through Craigslist and social media ads, referrals by the local harm reduction, and other participants. Interviews were conducted via Zoom. The interviews were transcribed and analyzed using NVivo.
Results: Participants were between 25 and 51 years of age, and 36% were female. 55% were non-Hispanic White, 32% Hispanic, and 14% of mixed ethnicity/race. Approximately 82% reported past 30-day use of heroin, and about the same percentage reported past 30-day use of non-pharmaceutical fentanyl in a counterfeit pill form. Nearly all participants reported changes in their drug use in the context of the COVID-19 pandemic. Participants discussed themes such as social isolation, boredom, lack of routine, and ease of hiding drug use from others as driving factors for their relapses and increased drug use. Some indicated that disrupted access to treatment due to COVID-19 restrictions perpetuated their drug use during the pandemic. Significant increases in the availability of fentanyl pills during the pandemic were linked to altered drug use

patterns, including shifts from injecting heroin to smoking fentanyl pills. A few participants reported decreasing drug use as a result of limited funds and changing social settings of drug use.
Conclusions: Circumstances surrounding the COVID-19 pandemic have created unique challenges for PWUO in Arizona. With the continuation of the COVID-19 pandemic and the increasing availability of fentanyl, these challenges are becoming more complex. Practitioners can begin to address these challenges by increasing access to treatment and expanding harm reduction efforts.
Financial Support: Arizona State University College of Health Solutions, COVID-19 seed grant.

W97. Kratom Use Among Pregnant and Postpartum Individuals With Substance Use Disorders

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Drug Category Other, krater
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: More than 10% of individuals with a substance use disorder (SUD) reporting lifetime use of Mitragyna speciosa (kratom), an herbal extract with opioid and stimulant properties. Kratom use in pregnancy is associated with maternal opioid withdrawal symptoms (OWS) and neonatal abstinence syndrome. However, the prevalence of kratom use among pregnant individuals with SUD is unknown. The aim of this study was to determine the proportion of pregnant and postpartum individuals with SUD who report use of kratom in pregnancy or lactation.
Methods: We conducted an anonymous, paper survey of individuals at the time of appointment with the University of Utah SUPeRAD clinic, a multi-disciplinary prenatal and postpartum clinic for individuals with SUD and/or chronic opioid use. We collected participants' demographic and pregnancy characteristics. We assessed lifetime kratom use, kratom use during pregnancy or lactation, and reasons for kratom use. Descriptive statistics were used to summarize the data.
Results: From January—May 2021, total of 80 respondents completed the survey with response rate of 81% (80/98). Fifty-three (66%) were pregnant and 27 (33%) were postpartum. Most identified as White (n=61, 76%). Most reported one or more chronic conditions: 66 (83%) one or more SUDs, 58 (73%) anxiety, 51 (64%) depression, 20 (25%) chronic pain, 12 (15%) migraines, 3 (4%) fibromyalgia or 14 (18%) other psychiatric conditions. In the entire cohort, 26 (33%) reported lifetime kratom use, 1 (1%) within past-month, 4 (5%) while pregnant, and 1 (1%) during lactation. Of the 26 respondents who used kratom, 16 used it for OWS relief (62%), 10 for relaxation (38%) 9 for pain control (35%), 6 for stress relief (23%) and 7 for other purposes (27%) (respondents may have more than one response).
Conclusions: In a survey of pregnant and postpartum individuals with SUD, 5% report kratom use in pregnancy and 1% during lactation.

W98. Umbilical Cord Homogenate Assay to Estimate Prenatal Kratom Exposure

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Drug Category Other, Kratom
Topic Prenatal/Perinatal
Abstract Detail Human
Abstract Category Original Research
Aim: Mitragyna speciosa (kratom), an herbal extract with opioid and stimulant properties, use in pregnancy is associated with maternal withdrawal symptoms and neonatal abstinence syndrome (NAS). In 2021, among US adults, the estimated prevalence of past-year kratom use was 0.8% [95% confidence interval (CI) = 0.7-0.9], however little is known about the prevalence among pregnant individuals. Drug assays of umbilical cord homogenate are used to characterize prenatal substance exposure particularly in late pregnancy. The aim of this study was to assess prenatal kratom exposure using mitragynine (MG) and speciociliatine (SC) positivity in a cross-sectional population-based sample of umbilical cords.
Methods: We randomly selected 657 samples from a total of 1748 previously collected umbilical cords from a 2020-2021 statewide prenatal substance exposure study in Utah. Kratom exposure was detected by

liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Umbilical cord segments were weighed, homogenized in acidified methanol solution with an internal standard, and centrifuged. Accuracy was assessed by spiking individual blank cords at the 50% and 150% control level. Supernatant was subjected to solid phase extraction and tested by LC-MS/MS for MG and SC concentrations exceeding the validated cutoff (0.08 ng/g).
Results: Of the 657 umbilical cord specimens tested, one umbilical cord tested positive at concentrations 2.6 ng/g MG and 4.9 ng/g SC. The calculated prevalence of kratom cord positivity was 0.2% (95% CI 0.0-0.8). All 50% control samples were below the cutoff concentration (0.08 ng/g) and all 150% control samples were above the cutoff concentration (n = 217). In all cases, retention time was within 2.5% of standard retention time and ion ratios were within 30% of standard values.
Conclusions: Based on 2021 Utah birth rates, over 1000 infants may be at risk of kratom-associated NAS.

W99. The Controlled Substances Act Regulations on Schedule I Researcher Registrations and the Need to Investigate New Substances of Abuse

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Drug Category Other, Schedule I Substances
Topic Other
Abstract Detail Human
Abstract Category Program Descriptions
Aim: The U.S. Controlled Substance Act (CSA) of 1970 established five schedules that classify controlled substances according to their potential for abuse and dependence, safety, and whether they possess legitimate medical value. Over fifty years later, the CSA, though amended on several occasions, remains the legal framework from which the Drug Enforcement Administration (DEA) derives its authority. One of DEA's responsibilities includes issuing researcher registrations to allow scientific and medical research to be conducted with controlled substances. The CSA has outlined different processes and requirements to conduct research with substances that are in schedule I versus II-V, with more requirements for schedule I substances. Substances are placed in schedule I based on having high potential for abuse, having no accepted medical use and lack of accepted safety for use under medical supervision at the time of scheduling (e.g., MDMA, THC, psilocybin, heroin, etc.). Conducting research with schedule I substances is critical to informing decisions. The CSA is not intended to be a deterrence to research. Research related to the harm or potential therapeutic effects of these substances, when done with adequate controls and procedures, ensures evidence based practices are employed.
Conclusions: Statistics about the schedule I researcher registration program, the process (along with guidance) on studying schedule I controlled substances will be outlined. Subjecting substances to a regulatory scheme protects research and disrupts unsafe promotion of such substances by traffickers prior to understanding their risks. Additionally, a list of substances associated with harm and are closely monitored by DEA will be provided.

W100. Drug Overdose Deaths in the United States and Brazil Between 2000 and 2018: A Comparison Analysis of Sociodemographics and Intentionality

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Drug Category Other, Opioids and Stimulants
Topic Disparities
Abstract Detail Human
Abstract Category Original Research
Aim: Drug use are on the rise in the Americas, and the two most populous countries in the region are the United States and Brazil. The patterns of drug use and overdose vary between both countries. We examined overdose records in these two countries from 2000 to 2018 and compared trends over time in overdoses and overall sociodemographic characteristics of deceased.

Methods: Using data from the National Center for Health Statistics for the US and from the Mortality Information System for Brazil, we identified records within 2000-2018 which the underlying cause-of-death was one of the following codes: X40–X45, X60–X65, or Y10–Y15. The US dataset includes 788,135 deaths, and the Brazilian 18,444 deaths.
Results: Drug overdoses deaths in the US and Brazil had similar mean ages (42·95 years and 38·82, respectively) and similar proportion of females (36·26% and 37·60%). They differed regarding race (86·96% of Whites and 43·97%), and intentionality of overdose (11·49% and 43·07 of intentional, 80·82% and 32·80 of unintentional). They also presented different trends over time regarding the gender (initial increase and posterior decrease in female percentage in the US and an overall decrease in Brazil) and race (initial decrease and following increase in non-White rate in the US and an overall increase in Brazil).
Conclusions: The different sociodemographic trends overdose deaths between in the US and Brazil must guide country-specific policymakers in their decisions. Nevertheless, data gathering must be improved with further training of coroners and more drug screenings to have high-quality data.
Financial Support: This study was funded by a pilot grant from the Columbia University President´s Global Innovation Fund.

DIGITAL POSTER PRESENTATIONS

Evaluating Loneliness and Binge Drinking Through a COVID-19 Follow-Up Survey Among Women in a Community Engagement Program in North Central Florida

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Drug Category Alcohol
Topic Epidemiology
Abstract Detail Human
Abstract Category Original Research
Aim: COVID-19 has elicited severe psychological distress among women as demonstrated by an increased prevalence of loneliness and excessive alcohol consumption. The objective of this analysis is to evaluate the relationship between self-reported loneliness (determined as low/medium/high) and binge drinking (yes/no) among women. We anticipate women who met the threshold for high loneliness would be more likely to binge drink compared to women with low loneliness.
Methods: Data were obtained through HealthStreet, a community engagement program in North Central Florida. Women aged 18+ in the HealthStreet cohort were interviewed during a COVID-19 follow-up evaluating thoughts on COVID-19 and associated health concerns (n= 2,061). Logistic regression models were performed, controlling for the following risk factors at follow-up: self-reported depression, self-reported anxiety, stress level, prescription pain medication use, age, food security, and employment status.
Results: Among the 14% of women who reported binge drinking, at least half reported medium stress levels (57%) and feeling anxious (49%) due to the COVID-19 pandemic. Being younger than 45 versus older had the greatest odds of binge drinking out of all risk factors evaluated (OR= 2.404, CI= 1.850, 3.124). Similarly, women who reported high loneliness had a higher odds of binge drinking than women who reported low loneliness (OR= 1.478, CI= 1.011, 2.159). Following age and high perceived loneliness, the next strongest risk factor for binge drinking included medium versus low perceived stress (OR=1.454, CI= 1.017, 2.078) and reporting depression (OR= 1.440, CI= 1.031, 2.012).
Conclusions: Though loneliness was not the strongest predictor of binge drinking, it was associated with binge drinking. The strongest risk factor for binge drinking was younger age; medium stress levels and depression were also associated with binge drinking. Interventions aimed at reducing binge drinking among women should focus on further understanding these risk factors and the effects of psychiatric comorbidities in association with binge drinking.
Financial Support: None; data were obtained through HealthStreet at the University of Florida

Reproductive History and Outcomes in the Young Women Arrested for Methamphetamine Use in Taiwan

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Drug Category Stimulants
Topic Sex/Gender Differences
Abstract Detail Human
Abstract Category Original Research
Aim: Taiwan has faced an alarming methamphetamine epidemic over the past decade. Methamphetamine involvement in women has been perceived as "double deviance"—against both formally-enacted laws and informal gender norms (e.g., mothers), which often act as barriers in recovery. The present study aims to characterize pregnancy history, outcomes, and associated factors in the methamphetamine-involved young women.
Methods: Building upon the 2000-2019 National Police Criminal Records, a total of 8147 women with ages under 30 arrested for methamphetamine were identified in Taiwan. A comparison group of women was ascertained at a ratio of 1:10 with matching on birth year and residential region (n= 81470). Information concerning sociodemographic characteristics, history of pregnancy and delivery, and pregnancy outcomes before the index arrest was obtained through data linkage with the National Health Insurance Database and National Birth Registration.
Results: Young women arrested for methamphetamine use were more likely to have a child (50% vs. 40%), have the delivery before the age of 20 (10% vs. 2%), have higher number of pregnancies (three or more: 10% vs. 4%), and underutilize prenatal. Methamphetamine arrest-related excess was also manifested in women's disadvantaged socioeconomic status (e.g., poverty and lower educational attainment) and adverse pregnancy outcomes (e.g., still births). Prior history of drug-related incarceration was slightly linked with increased risk of unfavorable trajectory of reproductive history.
Conclusions: Our results highlighted the urgency to integrate reproductive healthcare (and even childcare) when developing the community- and prison-based addiction treatment and rehabilitative programs delivered to women.
Financial Support: MOST 109-2629-B-010-001-MY3

A Spatial Science Approach to Inform Delivery of a Smartphone-Based Smoking Cessation Intervention

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Drug Category Nicotine/Tobacco
Topic Technology (e.g., mHealth)
Abstract Detail Human
Abstract Category Original Research
Aim: The ubiquity of smartphones provides an opportunity to create individually-tailored smoking cessation interventions with coping strategies delivered to smokers. The current study used ecological momentary assessment (EMA) data of smoking in combination with GPS data to inform when and where smoking cessation interventions should be delivered individuals.
Methods: Young adults (N=149, ages 18-26, 46% female, 39% non-Hispanic white) reported smoking and non-smoking events through a smartphone app for 30 days. We used a spatial science approach to identify individually-tailored hotspots of smoking in time and space to inform intervention delivery using geofences. For each participant, we aggregated Kernel Density Estimates (KDEs) to the Census-block level to compute mean KDEs for each block via Zonal Statistics. Block-level mean KDEs were normalized (0-1) to identify high-risk smoking areas. We sampled four participants based on the quartiles of total data available (smoking and non-smoking events) and plotted the percent of smoking events located within spatial geofences, regardless of time of day, to inform the sample-level normalized mean KDE threshold. High-risk blocks within daily 3-hour intervals were identified to create geofences (100-meter buffers around high-risk blocks) using the chosen threshold.
Results: Based on threshold sensitivity analyses for the four sampled participants, we chose a 0.3 threshold to generate spatiotemporal geofences. Depending on the participant selected, the geofences covered between 70%-100% of reported smoking events. The 3-hour intervals resulted in spatiotemporally dynamic geofences to improve individually-tailored interventions. Including participants at the 25% quartile of available data ensured this method is applicable for participants with low compliance with EMA data collection protocols.

Conclusions: This method can identify high-risk smoking situations by time and place and automatically generate individually-tailored geofences for smoking cessation intervention message delivery. Our approach will be applied in an ongoing R01 study to support young adult smoking cessation.
Financial Support: R01 CA246590; U01 CA154240; T32 DA007292

Building Organizational Capacity and Expertise to Treat Tobacco Dependence Within Behavioral Health Treatment Centers: A Qualitative Study of "Champion" Trainees' Perspectives of a Train-The-Trainer Program

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Drug Category Nicotine/Tobacco
Topic Treatment
Abstract Detail Human
Abstract Category Original Research
Aim: Aim: Behavioral health clients have elevated tobacco use rates and account for 50% of annual smoking-related deaths, yet rarely receive tobacco dependence treatment within behavioral health treatment centers (BHTCs). As lack of training and knowledge is a key barrier to providing tobacco dependence treatment, Taking Texas Tobacco-Free (TTTF) developed an iterative training and coaching train-the-trainer program to embed expertise and delivery of sustained education on tobacco-free policies and practices to participating BHTCs. Here, we explore "champions'" experiences and perceptions of the train-the-trainer program to adapt the program to local contexts, and to identify key factors contributing to successful program implementation.
Methods: Methods: We conducted 7 semi-structured, face-to-face interviews and 4 focus groups online (N=21), with 10 champions at 3 BHTCs, between July 2020–May 2021, pre- and post-implementation. Guided by thematic analysis and constant comparison, we inductively coded and summarized data into themes using an iterative process.
Results: Results: Data analysis yielded 5 factors contributing to successful program implementation: 1) Value of peer support and feedback; 2) Good communication, responsiveness, and practical coaching/ assistance by TTTF team; 3) Informative training curriculum, adaptable to targeted populations (e.g., intellectual/developmental disabilities, sexual minorities, homeless); 4) Staying abreast of current tobacco/nicotine research and products (e.g., e-cigarettes, SNUS, etc.); and 5) Building knowledge, increased champion confidence, and program ownership. Primary barriers included limited time resources– staff time constraints given heavy caseloads and competing priorities and certification trainings. While champions found the training program initially challenging, they all mastered the material and have integrated routine delivery of tobacco trainings into their BHTCs.
Conclusions: Conclusions: Champions reported that the TTTF train-the-trainer program was successful and identified practices, strategies and attitudes that can effectively build organizational capacity and expertise to sustainably address tobacco dependence within BHTCs. Study findings can guide and support other BHTCs in implementing sustainable tobacco-free workplace training programs.
Financial Support: Supported by: This project was supported by funding from the Cancer Prevention and Research Institute of Texas (PP200051 to L.R.R.).

Development and Process Evaluation of an Educational Intervention to Support Primary Care Based Sparing of Opioid Analgesics for Pain From New or Ongoing Non-Cancer Causes Among Opioid Naïve Patients

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Drug Category Opiates/Opioids
Topic Substance Use Disorder
Abstract Detail Human
Abstract Category Original Research

Aim: To describe the development and process evaluation of an audit and feedback (AF) intervention, designed to educate educate family physicians toto spare opioid prescriptions to opioid naïve patients in British Columbia (BC).
Methods: An AF intervention to improve safety of opioid prescribing in primary care has been launched in BC (www.ti.ubc.ca/portrait), with our assistance: mailing individual prescribing portraits to more than 5,000 eligible family physicians, followed by academic detailing webinars. The webinars' learning outcomes include defining the terms opioid naïve and opioid sparing and educating attendees on the (lack of) evidence for opioid analgesics to treat minor acute non-cancer pain. The primary outcome measure was a self-completion knowledge scale of four multiple-choice questions at the outset and conclusion of the webinar.
Results: A total of 200 participants attended four webinars and 124 (62%) responded to the knowledge questions. Participants were volunteers from community-based primary care (80/65%) and mostly urban settings (77/62%), who identified as family physicians (46/37%), nurse practitioners (24/19%), and residents (22/18%). Twelve participants (10%) recalled receiving the individualized portrait. While the correct identification of opioid naïve definitions increased by 23%, the correct identification of opioid sparing declined by 7%. An absence of supportive high-quality evidence for opioid analgesics and risk tools was recognized by 26% and 35% increased correct answers.
Conclusions: Training primary healthcare professionals in sparing opioid prescriptions for opioid naïve patients appears feasible. Along with the individualized prescribing portraits, the implementation strategies should utilize educational interventions to improve safety of opioid prescribing in primary care.
Financial Support: Canadian Institutes of Health Research

Leveraging SARS-CoV-2 Vaccination Efforts Through Latino MSM Drug Use and Sexual Networks

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Abstract Detail Human
Abstract Category Original Research
Aim: To describe the structure of drug use, friendship, and sexual networks among Latino men that have sex with men (LMSM) living in Miami, FL, and examine the extent to which dyadic drug use during the SARS-CoV-2 pandemic was associated with encouragement of SARS-CoV-2 vaccination.
Methods: Egocentric network data were collected from 48 respondents using quantitative Zoom assessments from August 2020-May 2021. Participants reported on their relationships with alters in 64 drug use dyads, 363 friendship dyads, and 119 sexual partner dyads. Bivariate associations were used to identify how drug use dyads could facilitate vaccination information dissemination, relative to sex and friendship dyads.
Results: Participants reported using the following drugs during the pandemic: cannabis (73%), cocaine (17%), sedatives (7%) and either stimulants, hallucinogens or inhalants (3%). With respect to types of networks, respondents reported feeling closer to members of their drug use networks (96%) than to their sexual network partners (73%) and friend network members (66%; $p<0.001$). A higher proportion of egos expressed a willingness to encourage their drug use alters to get vaccinated for SARS-CoV-2 (91%), relative to encouraging friends (86%) and sexual partners (82%). Egos in dyads based on drug use and sexual relationships were more confident in their ability to convince their alter to get vaccinated, if the alter was Latino (84% versus 55% non-Latinos; $p<0.001$).
Conclusions: In Miami, FL, a drug trafficking and SARS-CoV-2 hotspot, LMSM are more confident disseminating information about SARS-CoV-2 vaccination in drug use dyads than in friendship and sex dyads. Homophily based on ethnicity further strengthened this association, as Latinos were most willing to encourage vaccination among their drug use and sexual alters if the alters were also Latinos. The lessons learned from this study could be leveraged in future vaccination efforts or combined with peer-based harm reduction strategies within LMSM drug use and sexual networks.
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