1

IMPAIRED FRONTOSTRIATAL WHITE MATTER DEVELOPMENT IN CHILDREN WITH FAMILY HISTORIES OF SUBSTANCE USE DISORDERS.

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Aims: Children with family histories of substance use disorders (FH+) are at increased risk for developing substance use disorders relative to those with no such histories (FH-). We hypothesized that impaired development of frontostriatial circuits may lead to FH+ associated deficits in impulse control and related behaviors. We tested this hypothesis by comparing the integrity of frontostratial white matter in FH+ and FH- children using diffusion tensor imaging (DTI) prior to the onset of regular substance use.
Methods: White matter development was measured in FH+ (n=29) and FH- (n=12) children (ages 11-14) using a high (64-direction) angular resolution DTI sequence. Fractional anisotropy values where compared for the whole-brain average and cortico-striatal and prefrontal cortico-cortico tracts. Following group contrasts, these same measures were correlated with FH density, meaning the number of biological parents and grandparents with past or present drug or alcohol use disorders.
Results: FH+ children had less overall white matter development and lower FA values within cortico-striatal and prefrontal cortico-cortico tracts. Higher FH density was inversely correlated with both the whole-brain and regional FA values.
Conclusions: Our findings indicate that children with FH+ family history may experience impaired white matter development in the fronto-striatal tracts that this impairment is present prior to alcohol or other drug use. As part of our ongoing longitudinal project, we examine how these and other processes both predict and are influenced by onset of substance use.
Financial Support: R01-DA033997 and R01-DA026868

2

EVIDENCE FOR THE CONTRIBUTION OF D4 RECEPTORS TO COCAINE SELF-ADMINISTRATION IN MONKEYS.

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Aims: The effects of cocaine are primarily mediated by inhibition of monoamine reuptake, and the resulting stimulation of postsynaptic receptors. Dopamine receptors have been the focus of much study to determine their contributions to the effects of cocaine. However, the contribution of the D4 receptor has been challenging to study in part because of the absence of selective ligands. The aim of these studies is to elucidate this role, with the hypothesis that blockade of D4 receptors will reduce cocaine self-administration.
Methods: The NIDA Addiction Treatment Discovery Program has protocols for the blinded evaluation of compounds for efficacy in substance use disorders. One model uses rhesus monkeys trained to self-administer cocaine in a rapid extinction protocol using an FR30 operant schedule for both food and cocaine. In this paradigm, monkeys are trained to self-administer cocaine, and to quickly extinguish when saline is substituted. The protocol includes food-reinforced sessions before and after the availability of cocaine. Effects of a test compound can be evaluated across entire dose-effect curve of cocaine in groups of 4 male rhesus monkeys, and non-specific effects on responding for food are assessed. This protocol has been used to characterize a number of actual candidate medications as well as research tools, including dopamine D4 ligands buspirone, NGD 94-1, Ro 10-5824, and L 745,870.
Results: Dopamine D4 ligands modulated cocaine self-administration in rhesus monkeys. All of the ligands that were tested were effective in decreasing cocaine self-administration to different degrees, but efficacy to reduce cocaine self-administration was not related to receptor affinity or functional efficacy in vitro.
Conclusions: Issues with in vitro characterization of D4 will be discussed, but overall results suggest that D4 receptor blockade can modulate the reinforcing effects of cocaine and may be a future target for medication development.
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THE NEUROPSYCHOLOGICAL ASSESSMENT BATTERY (S-NAB) IN COCAINE-DEPENDENT PATIENTS.

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Aims: Cocaine abuse is associated with sub-clinical to severe cognitive deficits that may impair recovery. The Neuropsychological Assessment Battery-Screening module (S-NAB) is a comprehensive, modular test with normative data for adults that takes less time to administer than other comprehensive neuropsychological batteries. The S-NAB includes five modules: attention, language, memory, spatial and executive function. There have been few studies on the NAB using clinical samples. We present the index (composite) and individual test scores from the five core NAB cognitive modules in a sample of adult cocaine dependent individuals undergoing screening for cocaine treatment.
Methods: Participants were 90 current cocaine users presenting for an outpatient 12-week treatment study. Mean age was 45.7 (s.d., 6.2), 62% were male, 73% African-American, 52% had HS grad/GED. Participants had used cocaine regularly for a mean of 21.3 years (s.d., 7.6). At baseline, mean days of cocaine use per week in the past 30 days was 4.5 (s.d., 1.9). The S-NAB was administered to participants in one individual, 45-minute session.
Results: Of the sample, 30.3% performed at an average or better level across all cognitive domains, 29% performed below average but not impaired, and 40% performed in the impaired range. Using standardized scores of the five domains, performance on attention was significantly lower than language ($p=.02$), spatial ($p=.003$) and at a trend level for executive functioning ($p=.051$) but did not differ significantly from memory. Memory differed significantly from spatial ($p=.046$) and at a trend level from language ($p=.09$).
Conclusions: Performance on the S-NAB demonstrated by the current sample is consistent with the neuropsychological profile observed in clinical samples of adult cocaine dependent patients using longer batteries. Our study results that the S-NAB is an appropriate screening battery, appropriate for clinical settings where brevity of assessment and classifications of functioning is critical.
Financial Support: R01DA020647, K05 AA014223

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POLYDRUG USE AMONG EMERGENCY DEPARTMENT PATIENTS RECEIVING SBIRT SERVICES.

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Aims: This study describes the nature and extent of polydrug abuse among a population of emergency department (ED) patients identified as hazardous or harmful substance users.
Methods: 2184 adult ED patients, entering two academic EDs in Georgia, were enrolled in an evaluation study for a Screening, Brief Intervention, and Referral to Treatment (SBIRT) program. Upon entry into the ED, patients screening positive on a single alcohol or drug screening question received a comprehensive screen using the Alcohol, Smoking, Substance Involvement Screening Test (ASSIST). A score of 4 or higher for any substance was considered "at risk" use and prompted the delivery of a brief intervention aimed at reducing substance abuse. Descriptive statistics were used to quantify the prevalence of ED patients using 1, 2, 3, and 4+ substances in an "at risk" manner at some point prior to their entry into the ED. Analyses also describe risk levels of other substance use for patients presenting with harmful alcohol, cannabis, or cocaine use.
Results: Among patients with ASSIST scores high enough to warrant a brief intervention, 54% scored 4 or higher on a single substance, 31% were at risk for 2 substances, 11% were at risk for 3 substances, and 4 % were at risk for 4 or more substances. Further analyses determined the prevalence of specific drugs used concurrently. For example, among patients whose highest ASSIST score was for cocaine, 44% were also at risk cannabis users, and 67% were at risk alcohol users with 10% scoring in a range suggesting alcohol dependence (ASSIST of 27+).
Conclusions: Polydrug use is common among ED patients using alcohol or other drugs in a risky manner. Patients who scored highest on the ASSIST for cocaine have the highest rates of polydrug use: two in three are at risk for alcohol problems and almost half are using marijuana at a risky level. Practitioners delivering SBIRT services should prepare to address multiple substances in a brief intervention.
Financial Support: This project is funded by the Substance Abuse and Mental Health Services Administration
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DRUG-USING AFGHAN REFUGEES AND MOBILE UNIT SERVICES: A SUBPROJECT REPORT.

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Aims: Drug-using Afghan refugees are a socially marginalized group with an inadequate access to drug use treatment in Iran because of stigma and poverty. In 2011, a one-year outreach intervention was launched by Rebirth Society (NGO) with collaboration of the United Nations High Commission for Refugees (UNHCR) to implement free harm reduction services for impoverished Afghan refugees in slum areas of 3 cities in Iran. The current study aimed to describe the general profile of participants and the types of implemented services.
Methods: A well-equipped van was prepared as a mobile clinic. It was staffed by a group of 10 well-trained outreach street workers, doctors, and psychologists. Before starting the project, the outreach team identified and informed resident Afghans in the predetermined areas about the mobile unit services for 2 months. The mobile unit implemented its services from 7 am to 12 pm every day.
Results: During January-December 2011, 165 cases (163 men, 2 women) with mean age 24.8 (SD=9.1) years participated. 93.5% were opioid-dependent and 4.8% used methamphetamines. Main routes of drug administration included smoking (68.4%) and injection (19.2%). 3537 medical emergencies and visits were offered. 45 cases were referred to drop-in centers and night shelters. 169 family counseling sessions were held. 80 cases were referred to residential treatment and methadone therapy. 157 cases were referred for VCT counseling and serologic testing for HCV and HIV. 99 cases received training in safe sex. 21 cases received training in safe injection and 221 syringes and 8740 condoms were distributed.
Conclusions: Outreach interventions such as mobile units could be important options to reach impoverished Afghan refugees in Iran but further mobile unit services are still required in the country.
Financial Support: No financial support was received.

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A PRELIMINARY ANALYSIS OF AGGRESSIVE BEHAVIOR UNDER OXYTOCIN DOSE.

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Aims: Acute administration of oxytocin in human subjects has been shown to promote prosocial behaviors such as trust, generosity, and cooperation. Prosocial behaviors stand in contrast to antisocial behavior such as aggression. Aggression is an enduring problematic social behavior often resulting in deleterious consequences to criminal justice and public health systems. Aggression is prominent in antisocial personality disorder (ASPD), and exacerbated by the presence of a substance use disorder (SUD). The goal of this project is to investigate the acute effects of oxytocin (across three dose levels: 12IU, 24IU, and 48IU) on aggression in adult human subjects at high risk for aggression: those with ASPD and SUD. The hypothesis is that OT administration will decrease human aggressive behavior compared to placebo within this population.
Methods: Subjects aggressive responding is measured via the Point Subtraction Aggression Paradigm (PSAP), a well-validated laboratory measure of aggression, using a within-subjects counterbalanced design.
Results: Preliminary data suggest that aggressive responding has differential effects, based on subject's baseline (pre-dose) level of aggressive responding. Specifically, subjects with low levels of baseline aggressive behavior show an increase in aggressive behavior at the 24IU dose followed by decreased responding at 48IU. To date, changes in aggressive behavior did not correspond with increased physiological arousal or mood.
Conclusions: In our study aggressive responding under OT dose may vary based on baseline level of responding. Currently, the data suggests that subjects with low levels of baseline aggressive behavior show an increase in aggressive behavior at the 24IU dose of OT. Whereas, subjects with high baseline aggressive responding showed no difference from baseline; suggesting a ceiling effect. Across subjects changes in aggressive behavior did not correspond with increased physiological arousal or mood.
Financial Support: R01 DA 16965 P50 DA 09262

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ULTRA-RAPID SCREENING FOR SUBSTANCE-RELATED PROBLEMS USING THE ALCOHOL SMOKING AND SUBSTANCE INVOLVEMENT SCREENING TEST (ASSIST4).

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Aims: The ASSIST is a structured interview for adults attending primary health and welfare settings assessing alcohol, tobacco and other drug use and related problems. Three versions of ASSIST have been developed in international research but perceived lengthy administration deters routine use. In this study we test the hypothesis that a new short-form version can be developed.
Methods: 2,082 adults (18-62 years) recruited from general medical and specialist mental health services. Reference standards were current DSM-IV substance dependence and low-moderate versus moderate-severe tobacco dependence. Exploratory factor analysis and item-response theory models to identify and re-calibrated a core set of test items for each substance. Items were removed by diagnostic accuracy evaluation (area under the receiver-operating characteristic curve, sensitivity, specificity, positive and negative predictive values, kappa, likelihood ratios, and clinical utility index statistics).
Results: Successful isolation of a set of recalibrated test items for each substance. A test pair was isolated with diagnostic accuracy within an acceptable-to-excellent range (AUC [0.8-1.0], sensitivity [0.8-1.0], specificity [0.7-0.8], PVP [0.8-1.0], NVP [0.7-1.0], kappa [0.53-0.85], LR+ [2.5-5.9], LR- [0.0-0.2], CU+ [0.70-0.92], and CU- [0.45-0.76]). New item pairs were diagnostically more accurate than the longer form question for alcohol and tobacco, and non-inferior for cannabis, stimulants, sedatives and opioids (all AUC 0.79-0.93). On adjusted ROC curve analysis diagnostic accuracy was not significantly biased (moderated) by gender, age and recruitment setting, and with no evidence of differential diagnostic accuracy between countries.
Conclusions: ASSIST4 is an ultra-rapid clinical screening interview for alcohol, tobacco, cannabis, stimulant, sedative and opioid use and can be completed in two minutes or less.
Financial Support: Commonwealth Department of Health and Ageing, Australia.

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NEURAL MARKERS FOR RECOVERY IN CANNABIS WITHDRAWAL.

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Aims: Cannabis induced cerebral perfusion deficits are identifiable as reduced EEG spectral power in studies comparing users to non users. Previous work has shown that EEG band powers do not significantly increase during a 28 day abstinence, suggesting that cerebral perfusion deficits persist. This work uses EEG spectral phenotypes to explore recovery during withdrawal in the form of increases in spectral band powers.
Methods: A within subject case series of ten subjects with DSM-IV cannabis dependence as they go through two weeks of monitored abstinence from cannabis. Resting EEG measurements were taken for 2 minutes with eyes closed at two time points (before and after 14 days of abstinence), from frontal and occipital lobes using the international 10/20 electrode placement system (electrode sites AF3, AF4 and O1, O2) with the commercially available wireless Emotiv EEG headset. Artifact free EEG was converted to log band power in the frequency bands: Theta (4 – 7.9 Hz), Alpha (8 – 13.9 Hz), and Beta/Gamma (14 – 40 Hz) using a Fast Fourier Transform and analysed for changes from baseline to abstinence. Demographic, Drug Use and Withdrawal data were explored as predictors of change.
Results: None of the EEG frequency measures were significantly different between the baseline and withdrawal at either frontal or occipital lobes. Age at first cannabis use was a significant moderator of EEG power change in the Beta/Gamma frequency band (p=0.001).
Conclusions: The study found support for previous work showing that cannabis users do not show significant increases in EEG band power in any frequencies over a 14 day abstinence period. However, the study extends previous findings by demonstrating that the age at first cannabis use significantly moderates the recovery observed in Beta/Gamma EEG band power in frontal lobes during abstinence from cannabis.
Financial Support: This work was funded by the Australian Government Department of health and Aging, and by in kind support with the donation of the EEG headset from Emotiv Systems Ltd.

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HIV, HCV, HBV PREVALENCE AMONG HEROIN ADDICTS IN SAUDI ARABIA.

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Aims: 1-to calculate prevalence of HBV,HCV& HIV among inpatient heroin addicts in saudi central area.
2-Study the relationship between the Viral infections and some demographic variables.
Methods: Patients data had been collected from Alamal hospital in Riyadh, which is the only addiction treatment centre in the central saudi region & serve more than one third of saudi population . All patients whom admitted to inpatient services are screened of HIV antibody, HBV service antigen & HCV antibody & if positive, further confirmatory tests done in an external central laboratory. In this study i have reviewed heroin addicts inpatient's records whom were admitted between 31/1/2006 and 17/12/2009 . HIV, HBV, HCV results, age, number of admission, education, marital & occupational status were collected.
Prevalence of HIV, HBV & HCV and the associations between demographic variables & testing positive for these viruses were studied.
Results: 379 admission for 247 inpatient were analysed. All patient were male & more than 80% 0f them where admitted at least two times in their life. Prevalence of HBV, HCV & HIV are 9%, 82% & 10% consequently. Number of addmission, increase of age, being nonstudent with low education level are associated with increase testing positive of HCV. Divorced patients testing more positive of HIV & HCV than singles & married patients.
Conclusions: Heroin addiction prevalence in Saudi Arabi is not high & represent less than 7% of addmission to addiction centres, however this study prove that contracting serious contageous viral infection is very common among them & are similar to those among western addicts. HCV infection is twenty fold more in Saudi heroin addicts than in general population while HIV infection is more than six hundred fold & infection with HBV is just a little bit more than that in general population. Infection control, education & harm reduction are of paramount importance in dealing with this problem. Opioid maintainance medication are not licenced in Saudi Arabia & even naltrexone is not available, though this model of intervention could be of great help in dealing with such an issue.
Financial Support: none

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MALADAPTIVE CORTICAL SEROTONIN (5-HT) 5-HT2A:5-HT2C RECEPTOR BALANCE GENERATES ABERRANT IMPULSIVITY AND ELEVATED COCAINE CUE REACTIVITY.

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Aims: The cycling nature of cocaine dependence stymies efforts to stay abstinent with vulnerability to relapse oft precipitated by high impulsivity and reactivity to cocaine-associated cues. There is considerable evidence that 5-HT systems play a role in impulsivity and cue reactivity through 5-HT-receptive proteins found in frontal cortex. We tested the hypothesis that these interlocked phenotypes are rheostatically controlled by 5-HT2AR:5-HT2CR homeostasis within the medial prefrontal cortex (mPFC).
Methods: Impulsivity and cue reactivity were evaluated in rats using the the 1-choice serial reaction time task and cocaine self-administration (SA) and forced abstinence (FA) paradigm, respectively. We employed immunoblots to detect the mPFC synaptosomal expression of 5-HT2AR and 5-HT2CR of phenotypically differentiated rats. Disruption of the 5-HT2AR:5-HT2CR balance was achieved following genetic deletion of the 5-HT2CR in the mPFC; rats were then subjected to behavioral tests.
Results: High impulsive rats exhibit a higher 5-HT2AR:5-HT2CR protein ratio in synaptosomes from mPFC vs. low impulsive rats ($p<0.05$). Rats with a knockdown of 5-HT2CR in the mPFC expressed significantly elevated impulsive action relative to control rats ($p<0.05$) and enhanced potency of the 5-HT2AR antagonist M100907 to suppress impulsive action ($p<0.05$). In rats trained to SA cocaine (0.75 mg/kg/inf; FR5; 14 days) and then assessed for cue reactivity on FA Day 1 or FA Day 30, we observed elevated cue reactivity and a late-forming increase in the 5-HT2AR:5-HT2CR mPFC synaptosomal protein ratio at FA Day 30 ($p<0.05$).
Conclusions: These data indicate that there is a reciprocal or interactive relationship between 5-HT2AR and 5-HT2CR, notably in mPFC, that is key in expression of these phenotypes, and that a 5-HT2AR:5-HT2CR imbalance may be a functionally-relevant mechanism underlying impulsivity and cue reactivity.
Financial Support: DA06511, DA024157, DA000403

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NOVEL ASSOCIATION OF AMGYDALA PRODYNORPHIN WITH ADDICTION AND NEGATIVE AFFECT-RELATED NEUROCIRCUITRY.

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Aims: Negative affect plays a significant role in conferring vulnerability to drug addiction. Rodent models of addiction and depression point to amygdala Prodynorphin (Pdyn) as a candidate substrate yet, its clinical relevance is unknown. Aim 1 focused on assessing PDYN mRNA expression in the post-mortem human amygdala of drug addiction or Major Depressive Disorder (MDD) subjects. From these studies, we found that these cohorts have a mutual reduction of PDYN in the amygdala sub-nucleus, the Peri-Amygdaloid Cortex (PAC). To gain insight into the functional role of this disturbance, Aim 2 focused on mapping the functional neurocircuitry of Pdyn neurons in the PAC.
Methods: Using in situ hybridization histochemistry, PDYN mRNA expression was examined in the post-mortem human amygdala of three cohorts: (1) a multidrug (n=22); (2) heroin (n=46) and (3) MDD (n=24). Pdyn expression was also assessed in rodents (n=28) from the chronic heroin self administration paradigm. Targeted viral strategies that inhibit Pdyn neurons in the PAC were paired with PET imaging to map the functional circuits relevant to this inhibition.
Results: Our results demonstrated that human drug addiction and MDD subjects have a common reduction of PDYN mRNA expression in the PAC. Given this shared change and the unknown functional role, we examined Pdyn mRNA expression in the PAC using a rodent model of heroin abuse and found that chronic heroin self-administration led to a similar reduction. Next, we pursued functional whole brain mapping of circuits related to the inhibition of Pdyn neurons in the PAC and found that this inhibition conversely led to the activation of the extended amygdala. Physiological responses due to the activation of this stress circuit were also evident.
Conclusions: Using a translational approach, our results have identified a novel neurobiological substrate related to the brain's stress system that is pertinent for understanding the high comorbidity rate of drug addiction with affective disorders.
Financial Support: DA15466

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CHRONIC TREATMENT WITH ETHANOL-ENHANCED MORPHINE-INDUCED HYPERLOCOMOTION.

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Aims: It is well known that ethanol has dependence potential, and the endogenous u-opioid receptor system is involved in the reinforcing/rewarding effects of ethanol. It has been reported that the psychological dependence on morphine could be easily developed in patients who have ethanol dependence history. Several studies have investigated the role of the mesolimbic dopaminergic system in the reinforcing/rewarding effects of ethanol and morphine. However, the exact mechanism how ethanol treatment can affect the development of psychological dependence on morphine is not elucidated yet. Therefore, the present study was designed to investigate the chronic treatment with ethanol on the activation of dopaminergic system induced by morphine as measured by locomotor activitiy.
Methods: Mice were treated with liquid 3% ethanol diet for 5 days. All experiments were conducted after 3 days withdrawal period in mice treated with ethanol. The locmotor activity of mice was measured by tilting-type cage. Total activity counts were automatically recorded for 3hr after morphine (5mg/kg, s.c.) treatment. Brain tissue was prepared for biochemical assays at 0-hr, 6-hour, 12-hr and 24-hr after ethanol withdrawal.
Results: We found that chronic treatment with ethanol significatly enhanced morphine-induced hyperlocomotion($F(5,5.5)=5,823, P<0.05$) suggesting that ethanol modify several neuroprastical or moleculer events in the central nervous system. Here the GSK3β protein levels were significantly increased, whereas protein levels of p-Akt, a controlling element of GSK3β, were decreased in the ventral tegmental area, projection area of the mesolimbic dopaminergic system after chronic treatment with ethanol.
Conclusions: These results suggest that morphine-induced hyperlocomotion was enhanced by chronic treatment with ethanol, and alternation of p-Akt/GSK3β passway, which has crucial element for neuroplastical change, is involved in the enhanced mesolimbic dopaminergic system after chronic ethanol treatment.
Financial Support: Suzuki Tsutomu

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SLEEP AND CLINICAL OUTCOMES IN THE PLACEBO ARM OF A RANDOMIZED CLINICAL TRIAL OF MODAFINIL TREATMENT FOR COCAINE DEPENDENCE.

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Aims: To describe polysomnographic (PSG) and self-report sleep changes and relate them to clinical outcomes.
Methods: Results are presented from 16 participants who were randomized to receive placebo, in an ongoing clinical trial. Treatment consisted of 12 days of standard inpatient substance abuse treatment followed by 6 weeks of outpatient cognitive behavioral therapy and thrice weekly urine toxicology. Sleep PSG was performed during the first and second inpatient weeks and during the 3rd and 6th outpatient weeks. PSG data were analyzed based on study day and number of days abstinent at the time of measurement. Participants completed sleep and substance use questionnaires throughout the study.
Results: PSG results replicate earlier findings with low slow wave sleep (SWS) times and decreasing total sleep time (TST) with abstinence. Preliminary evidence suggests that TST and to a lesser degree SWS time begin to rebound after 2-3 weeks of abstinence (quadratic models outperformed linear models with $p < 0.0001$ and $p = 0.051$ for TST and SWS, respectively). Change in SWS from the first to second weeks predicted abstinence (maximum number of consecutive days abstinent; $R=0.52$; $p = 0.056$; two tailed). Stability in bed-time during the outpatient phase also correlated with abstinence ($R = 0.53$, $p = 0.051$; two tailed).
Conclusions: This study suggests a "u" shape trajectory of the TST and SWS in which they decrease in the initial period abstinence and increase afterwards. Notably, increases in SWS and stability of sleep schedule correlated with abstinence, suggesting the potential importance of sleep architecture and sleep regulation in relapse.
Financial Support: NIDA (R01DA011744) and the State of Connecticut, Department of Mental
Health and Addiction Services.

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EARLY DROP-OUT: AN INDICATION OF TREATMENT SUCCESS OR DIFFICULTIES?

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Aims: Previous discussion has suggested that early drop-out may not indicate negative outcomes, but early treatment success. Using data from a recently completed pharmacotherapy trial, this study compares participants who did and did not participate in both of two consecutive treatment phases to examine early drop-out.
Methods: 202 opioid-dependent participants were offered 16 weeks of buprenorphine and random assignment to behavioral treatment condition (Phase 1), followed by 16 weeks of medication-only treatment (Phase 2). Outcomes reported here compare the group that completed Phase 1 and began Phase 2 (GP2, n=134) with the group that began Phase 1 but did not begin Phase 2 (GP1, n=69). Additionally, Phase 1 and Phase 2 opioid use and retention were compared in the GP2 group to address whether treatment performance improves with time in treatment.
Results: No differences in baseline demographic characteristics between GP1 and GP2 were found, however GP2, as compared to GP1, reported significantly fewer days of heroin use in the last 30 days (13.2 days vs. 19.4 days, $p=0.002$), and significantly more days of other opioid use, such as prescription opioids (14.2 days vs. 8.1, $p=0.002$). The GP2 group also had a significantly lower percentage of opioid-positive urine test results at baseline (74.6%) compared to the GP1 group (91.2%) ($p=0.005$). During Phase 1, GP2 had a significantly greater percentage of opioid-positive urine tests (0.69, sd-.44) than the GP1 group (0.53, sd = 0.49) ($p < 0.05$). Comparing GP2 Phase 1 and 2 performances, no significant difference was found in opioid use, percent retained in the phase, or mean number of weeks retained.
Conclusions: Baseline drug use differences suggest that the GP1 group had more severe drug use than GP2. The GP1 group also used opioids in the first treatment phase significantly more than GP2, suggesting that drop-out was not due to early treatment success. The performance of the GP2 group did not differ between the two treatment phases indicating that treatment performance was steady, suggesting that early engagement may be critical for retention and optimizing treatment success.
Financial Support: NIDA DA020210

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IMPAIRED NUTRITIONAL STATUS AND POOR DIET QUALITY AMONG METHADONE MAINTENANCE PATIENTS.

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Aims: Comprehensive methadone maintenance treatment (MMT) should ideally address co-occuring disorders and behaviors. To explore the relation of these issues, we analyzed the nutritional status and lifestyles during MMT. This study characterized the association of methadone dose, psychosocial and lifestyle factors with outcomes of nutritional status and diet quality.
Methods: Seventy-six patients (at least 6 months in MMT) gave consent. Demographic variables, mean arterial pressure, and waist/hip ratio were collected along with measures of depression, smoking, perceived stress, anxiety, addiction severity, insomnia, exercise, eating patterns, and delay discounting. A correlational analysis was conducted between these variables and Healthy Eating Index score (HEI-2005; a measure of diet quality), body mass index (BMI; a marker of nutritional status), and 24-hour caloric intake.
Results: Mean age was 46 years; 57% male. 54% of subjects were African American, 45% Caucasian, and 1% Native American. Mean BMI was 30 kg/m2 (obese). Mean HEI-2005 score was 47 out of 100 (U.S. mean 61). Variables significantly correlated with HEI-2005 score were: methadone dose (-0.326; $p=0.0008$), ASI social component, (-0.378; $p=0.003$), ASI psychiatric component (-0.333; $p=0.009$), State Anxiety (-0.261; $p=0.037$), and Beck Depression Inventory(-0.252; $p=0.043$). BMI only correlated with Trait Anxiety (-.278; $p=.036$); 24-hour caloric intake had no correlations.
Conclusions: The mean BMI score suggests an impaired nutritional status amongst methadone patients. HEI-2005 scores demonstrate low diet quality among MMT patients and were inversesly correlated with methadone dose, components of addiction severity, and ratings of anxiety and depression. Future analyses will explore the relative contribution of these variables to healthy eating, and the possible mediating factors for directionality of effects observed. Research should be conducted on the effectiveness of interventions during MMT that address poor diet quality and associated factors (e.g., anxiety).
Financial Support: NIDA K24DA023186

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PARENTAL ABSENCE AND MARIJUANA USE AMONG AMERICAN YOUTH IN THE LATEST NSDUH.

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Aims: Economic and technological changes have impacted the structure and functionality of the American family. In the present study, we inquire whether the older than 50-year old findings from the 1960's about parental influence on children's risk of substance use hold in this age and stage.
Methods: The data are from the most recently released National Survey on Drug Use and Health 2010, (n=57831, subpopulation, 18601). For focus, the analyses are restricted to participants 12-17 years. Regression models accommodate the complex sample design, with attention to sampling weights and clustering by primary sampling units via STATA svy commands.
Results: Compared to youth who live with both parents, those who live with either or neither had greater odds of ever using marijuana (OR=1.6, 95% CI = 1.4-1.8 for father only; OR=, 1.8, 95% CI = 1.4-2.2 for mother only; and, OR=2.5, 95% CI = 1.7-3.0 for neither parent, all $p<0.001$), controlling for race/ethnicity, income, and gender. No difference in age of first use was observed in relation to parental absence ($p> 0.661$). Again comparing to those who lived with both parents, youth who lived with their father only had 1.6 higher odds of marijuana use in the past month (95% CI= 1.3-2.0, $p < 0.001$), those who lived with their mother only had also higher odds (OR=1.7, 95% CI = 1.3-2.7, $p=0.001$), and those who lived with neither parent had the highest odds of marijuana use in the past month (OR= 2.0, 95% CI = 1.1-3.8, $p=0.030$).
Conclusions: As expected, youth who lived with both parents had lower odds of marijuana involvement. However, the mechanism through which parental presence deters initiation of marijuana is not clearly understood and needs further research. Findings of this study add to the base for targeted interventions for adolescents from single-parent households, including mentorships and more after school programs.
Financial Support: IDA grants DA012390 and DA019805

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BUPRENORPHINE-NALOXONE INDUCTION-DOSING PREDICTS TREATMENT OUTCOME.

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Aims: The European SPC for buprenorphine-naloxone (BNX) recommends an induction dose of 8mg/day and a slow increase to a maintenance dose of 24mg/day. Clinical studies have shown impressive retention rates and improvements in health and social circumstances in patients with much higher induction and maintenance doses. The aim was to examine to what degree induction dosing predicts treatment outcome.
Methods: Data from a prospective, observational study with BNX conducted at N=69 sites with N=337 eligible datasets was analysed. With the maximum dose of the first 7 days of BNX treatment the low-dose (LD: ≤8mg/day), medium-dose (MD: >8-16mg/day) and high-dose (HD: >16mg/day) group was created. All analyses were conducted using STATA/SE 9.0.
Results: The probability to retain in therapy with BNX was significantly higher in the LD group. They were more likely full-time employed, lived in their own flat and received take-home prescription. They were less burdened with withdrawal, craving and psychiatric distress. General health and quality of life were significantly better. The HD group had the worst condition in almost all rates and scores evaluated at baseline.
All patients showed significant improvement in social, physical and psychiatric variables during therapy with BNX. The highest improvements were found in the HD group.
Conclusions: Physicians seem to allocate their patients to a certain induction dose with respect to specific patient characteristics such as social circumstances, physical and mental health, withdrawal and craving. The higher probability for treatment retention in the LD group might be explained by the fact, that these patients start their therapy from a superior level. Although patients in the HD group have a lower chance to be retained, completer showed significantly higher improvements compared to the LD group. These findings suggest that higher induction doses contribute to treatment success significantly.
Financial Support: Essex Pharma GmbH & Reckitt Benckiser were Sponsor of the study. S. M. Apelt receives or has in the past 3 years received honoraria from: Schering Plough, Essex Pharma GmbH, MSD SHARP & DOHME GmbH and Reckitt Benckiser Pharmaceuticals.

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HOW SUBSTANCE USE CAN AFFECT HIV TEST RATES FOLLOWING A COMPUTER-BASED VIDEO INTERVENTION.

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Aims: To increase HIV test rates in a high volume hospital emergency department, and examine how substance use may interact with HIV testing behavior.
Methods: 160 emergency department patients who declined HIV tests at triage viewed a computer-based video intervention designed to increase test rates. The intervention took < 16 minutes to complete and included a brief automated substance use screening based on the WHO ASSIST. At the end of the intervention, computers asked patients if they would like an HIV test. A subset of participants (n=40) was interviewed afterward.
Results: One-third (33%, n=53) of participants accepted a test at the end of the intervention; 37% reported using drugs other than tobacco or alcohol in the last three months. 10% reported that a friend or family member had ever expressed concern about their drug use, 13% reported they had ever tried and failed to control, cut down, or stop their drug use. 13% reported that drug use had caused them legal or financial problems in the past three months. In interviews, participants said they felt more comfortable disclosing substance use to a computer than to a person who they felt might make negative judgments.
74% reported alcohol use in the past three months, 33% reported weekly or daily use. Participants who reported they tried to curtail alcohol use and failed (15%) were more likely to accept an HIV test compared to others in the sample (54% vs. 30% tested; $\chi 2 = 5.04$, $p < .05$). Those who reported friends or family had expressed concern over their alcohol use (15%) were also significantly more likely to accept a test ($\chi 2 = 3.84$, $p < .05$).
Conclusions: These data suggest that integrating computer-based screening with an intervention facilitates substance use disclosure and increases the likelihood that HIV-test averse ED patients would agree to testing. Integrating routine computer-based screenings with brief targeted interventions may enable better understanding of how reported substance use may influence response to behavioral interventions.
Financial Support: NIDA R03DA031603, NIDA P30DA029926

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EVALUATION OF SELF-EFFICACY TO USE HARM REDUCTION STRATEGIES AMONG MARIJUANA-USING UNIVERSITY STUDENTS.

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Aims: Given the frequent and periodically excessive use of marijuana by university students, many could benefit from employing harm reduction strategies to prevent or reduce the unhealthy consequences of using marijuana. Our primary aim was to assess how confident regular marijuana users were that they could use each of 18 specific strategies to reduce negative outcomes that may result from use.
Methods: Using a web-administered questionnaire designed as part of this study, we evaluated 272 university student marijuana users' confidence they could use each of 18 different harm reduction strategies as a function of their previous experience of marijuana-related problems (based on Rutgers' Marijuana Problem Index).
Results: We found that participants in the group with the highest problem scores reported lower self-efficacy compared to the moderate problem score group on 8 of the 18 strategies (e.g., "Avoid going to work or school while high," "Avoid using marijuana to help you sleep," "Avoid driving or cruising while high"). In addition, the highest problem score group had lower self-efficacy compared to the low problem score group on all strategies except for two (i.e., "Use a vaporizer instead of smoking marijuana," Eat baked goods that contain marijuana instead of smoking it"). Calculating total scale self-efficacy across all 18 strategies, we found that overall harm reduction self-efficacy was positively associated with refusal self-efficacy in a variety of contexts, and negatively associated with the number of marijuana-related problems, but was not significantly associated with past 30-day use of marijuana.
Conclusions: Clinicians and educators could use this list of harm reduction strategies to identify clients who might benefit from encouragement and training to employ specific strategies in high-risk situations, and to assess changes in confidence to engage in specific harm reduction techniques as an outcome of public health education.
Financial Support: N/A

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CHANGES IN UNDERSTANDING OF OPIOID-INDUCED HYPERALGESIA-CLINICAL IMPLICATIONS.

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Aims: Aims. Describe growing recognition 1. Chronic pain patients, treated with opioids, may develop addiction and a greater sensitivity to pain (hyperalgesia) than generated by original pathology 2. Opioid addicts maintained on opioids may also develop hyperalgesia 3. Hyperalgesia and opioid tolerance may be separate mechanisms
Results: Supported by changes in understanding. 1 Previously thought methadone and buprenorphine maintenance provided analgesia. Subsequently disproved. 2 Previously thought methadone or buprenorphine produced hyperalgesia and opioid analgesic tolerance (tolerance) seen in opioid addicts. Research shows patients prior to entering opioid substitution treatment hyperalgesic as consequence of initial opioid addiction (e.g. heroin or prescription opioids) or earlier predisposition 3 Previously thought hyperalgesia and tolerance of methadone and buprenorphine patients different. Research shows hyperalgesia and tolerance similar in these patients. 4 Previously thought opioid treatment in context of pain did not induce hyperalgesia and tolerance. Research shows non-cancer chronic pain patients maintained on opioids for pain management develop similar hyperalgesia to patients on opioids for addiction treatment. 5 Previously thought abstinence 'reset' hyperalgesia and tolerance. Research shows former opioid addicts remain hyperalgesic following abstinence. 6 Previously thought hyperalgesia basis for tolerance. Research shows while opioid addicts remain hyperalgesic following abstinence, tolerance to other effects (e.g. respiratory) rapidly attenuate and potentially fatal. Therefore postulate different mechanisms.
Conclusions: Conclusion. Clinical implications for improving patient care. Consent forms prior to maintenance on opioids describing risks and implications of hyperalgesia development. Management plans for post-surgical pain relief. Research shows increased use of opioids, in combination with non-opioid approaches (total 2.5 times morphine equivalents) provides pain management following surgery.
Financial Support: Nil

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10-YEARS OUTCOME OF METHADONE- AND BUPRENORPHINE-MAINTAINED PATIENTS. MORTALITY, QUALITY OF LIFE AND SUBSTANCE USE.

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Aims: The objective of this study was to describe the 10-years outcome of Opiate use disorder patients initially assigned to methadone or buprenorphine maintenance treatment.
Methods: Opiate use disorder patients in Methadone and Buprenorphine treatment who completed the 10-year follow-up assessment of an ongoing follow-up study were selected. Participants were assessed every 6 months with the Addiction Severity Index (ASI) and the Nottingham Health Profile (NHP) to assess the Quality of Life. We described the retention in treatment, the death rate and the changes in ASI and NHP scores (MANOVA).
Results: 187 patients were selected (73% males, 31.4 y.o.). At baseline 120 (64%) received methadone and 67 (36%) buprenorphine. At 10-year follow-up, 15 (8%) had died (13 methadone, 1 buprenorphine and 1 out-of-treatment) ($\chi 2$= 2.84, p= .09). Among the 172 patients alive after 10 years, 40 received buprenorphine, 104 methadone and 28 had stopped treatment (after an average time in treatment of 36 months). Patients in buprenorphine treatment (n=11, 22%) stopped treatment more than those in methadone (n=17, 14%) ($\chi 2$= 17.66, p= .0001). Over the 10-year period, the use of substances (opiates, alcohol (5+ units), benzodiazepines, cocaine, cannabis) significantly decreased except for alcohol (any use) and tobacco. All the ASI severity scores showed an improvement but only the Drug score reached significance (F= 14.90, p= .0008). The NHP scores exhibited improvement in Quality of life for Sleep (F= 4.57, p= .04) and Emotional Reactivity (F= 10.62, p= .003).
Conclusions: In comparison to previous studies, this sample showed a low death rate at 10-year follow-up and confirmed the effectiveness of opiates maintenance treatment to reduce substance use and to improve quality of life. Larger samples are needed to compare the 10-year outcomes regarding the length in treatment.
Financial Support: PHRC 1994, 2000, 2006, MILDT-INSERM 2004 and Reckitt Benckiser 2011

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ABUSE POTENTIAL AND ANALGESIC EFFECTS OF OXYMORPHONE IN PRESCRIPTION OPIOID ABUSERS.

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Aims: Oral formulations of oxymorphone (Opana®, Opana ER®), a mu opioid analgesic indicated for moderate-to-severe pain relief, were approved for use in the U.S. in 2006. Since that time, abuse of oxymorphone has escalated; however, there are limited controlled data available on its pharmacodynamic profile. The study aims were to examine the pharmacodynamic profile, including subjective, physiological and analgesic effects, and the relative potency of oxymorphone in comparison to oxycodone.
Methods: Healthy, non-dependent prescription opioid abusers were enrolled as inpatients in this within-subject, double-blind, placebo-controlled, 3-week study. A total of 7 experimental sessions (6.5 hr) were conducted; during each session an oral dose of oxymorphone (10, 20, 40 mg), oxycodone (10, 20, 40 mg) or placebo was administered. Outcomes were assessed before and repeatedly after dosing, including physiological indices, standard abuse liability questionnaires and two tests of experimental pain (i.e., the cold pressor test and pain pressure algometer).
Results: Findings, to date, reveal that oxymorphone (40 mg) and oxycodone (40 mg) produce equivalent miotic effects (mean trough values = 2.4 and 2.3 mm, respectively), comparable ratings on prototypic subjective indices of abuse potential (e.g., "drug liking," "high"), and equianalgesic effects on the cold pressor test. However, at identical lower doses (10 & 20 mg), oxycodone produces effects of greater magnitude compared to oxymorphone for most measures, with 10 mg oxymorphone appearing placebo-like.
Conclusions: These data suggest that, while oxymorphone and oxycodone produce a similar profile of action at higher doses, the dose effect curves are not parallel due to the limited activity of oxymorphone at the lower doses. The finding of a steep dose response function for oxymorphone may be predictive of a comparatively narrow safety index.
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EFFECT OF GENDER ON PAIN SENSITIVITY AND TOLERANCE IN ADOLESCENTS DURING ACUTE ABSTINENCE.

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Aims: There is a paucity of research on gender differences in pain perception between smoking and non-smoking adolescents and how these differences impact cessation attempts. As such, we aim to elucidate gender differences between smokers and non-smokers in pain sensitivity (PS) and pain tolerance (PT) during acute abstinence. We also examine the impact of withdrawal and craving on pain during acute abstinence.
Methods: Ninety-six adolescents (53 smokers, 43 non-smokers) aged 14-18 years were recruited to participate in a non-treatment inpatient trial characterizing nicotine withdrawal. Participants were abstinent from smoking from admission to discharge (48hrs). They engaged in the Cold Pressor Task twice to assess PS and PT. Throughout the task, pain ratings, blood pressure, heart rate and salivary cortisol were measured. Withdrawal and craving were assessed prior to, and following completion of, the Cold Pressor Task.
Results: ANOVA regression analyses were used. Age at trial participation differed significantly between smokers and non-smokers. Thus, analyses were adjusted for age. Smokers felt pain more quickly following hand submersion (smokers-35.60 ± 25.10 v. non-smokers-63.0; p<0.001) and removed their hands from the water more quickly (smokers-41.76 ± 25.71 v. non-smokers-56.80 ± 25.49; p=.0039) than non-smokers. Female smokers demonstrated decreased overall hand submersion time as compared to non-smoking females (smokers-32.24 ± 23.78 v. non-smokers-59.75 ± 25.39; p=.0121).
Conclusions: Smokers had significantly higher pain sensitivity and lower pain tolerance than non-smokers. Additionally, female smokers demonstrated greater decrements in pain tolerance than female non-smokers. Female smokers may experience greater levels of discomfort during acute abstinence, which may in turn increase their likelihood of relapse. This highlights an additional target for cessation intervention.
Financial Support: Supported by NIDA grant # R01HD37688

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UNDERREPORTING OF DRUG USE AMONG INDIVIDUALS WITH SCHIZOPHRENIA: PREVALENCE AND PREDICTORS.

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Aims: Illicit drug use is common in individuals with schizophrenia, and it has been suspected that many individuals underreport their use of substances, leading to significant barriers to treatment. This study sought to examine the degree to which individuals with schizophrenia disclose their use of drugs on self-rated assessments, as compared to laboratory assays, and determine the contributors of underreported drug use in this population.
Methods: A total of 1042 individuals with schizophrenia who participated in screening/baseline procedures for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study completed self-rated assessments of substance use and laboratory drug testing. Laboratory tests assayed cannabis, cocaine and methamphetamine use; the procedures included radioimmunoassay (RIA) and urine drug screens.
Results: A significant proportion of participants tested positive for drug use on laboratory measures (n = 397; 38.0%), and over half (n = 229; 58%) did not report using these drugs. Logistic regression models confirmed patients who were most likely to conceal their use tended to be older, and presented with greater neurocognitive deficits. Patients who accurately reported drug use tended to have greater involvement with the criminal justice system. Illness severity and psychopathology were not associated with whether patients disclosed drug use.
Conclusions: Rates of underreported drug use are considerable among individuals with schizophrenia when compared to laboratory assays, and the exclusive reliance on self-rated assessments should be used with caution. Patients who underreport their drug use are more likely to manifest neurocognitive deficits, which should be targeted by interventions attempting to optimize treatment.
Financial Support: National Institute of Health grants DA-30763(SME) and RR-24154(SME).

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SYNERGY OF GROUP III MGLUR-SELECTIVE AGONIST AND MORPHINE IN SENSITIZED PERIPHERAL FIBERS.

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Aims: Morphine is widely used to treat acute and chronic pain. However, deleterious side effects occur when it is used at length or in high doses. Current studies seek to establish receptor groups and agonists that potentiate analgesic efficacy of morphine, allowing use of lower doses to decrease side effects. Thus, metabotropic glutamate receptors (mGluRs) are of interest. Current literature indicates that intrathecal and systemic applications of Group III agonists potentiate morphine analgesia. Previously, we demonstrated that intraplantar application of a Group III agonist (L-AP-4) synergistically potentiates morphine anti-hyperalgesia in a rat model of peripheral inflammatory pain and that the Group III mGluR8 and mu opioid receptor co-localize in 28-55% of rat DRG nociceptors. In this study, we sought to determine if the combination decreases sensitization at the single fiber level.
Methods: We employed the in vitro skin-nerve preparation in which the medial and lateral plantar nerves are dissected and kept intact with the skin of the hindpaw. Then, individual fibers were sensitized to heat via application of inflammatory soup (5-HT, PGE2, bradykinin, histamine), and either morphine or L-AP-4 was applied to obtain a dose response curve for each drug.
Results: Dose response curves for each drug were gathered and used to identify individual IC50s (208uM morphine; 0.54uM L-AP-4; n=6-31 fibers). Each IC50 was then divided by 1, 2, 4, 8, and 16 to determine the combination doses for morphine plus L-AP-4 (M+L: 208uM+0.54uM; 104uM+0.27uM; 52uM+0.135uM; 26uM+.068uM; 13uM+.034uM).
Conclusions: Additional study will involve applying combination doses to sensitized fibers to determine if the Group III agonist synergistically potentiates morphine. We will assess synergy by conducting isobolographic analysis. Overall, we expect that peripheral Group III mGluR activation will synergistically potentiate morphine-induced inhibition of inflamed peripheral fibers.
Financial Support: NIH F30DA03229801 to ALB; NS027910/DA027460 to SMC.

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WHOSE POST-TRAUMATIC STRESS AFFECTS DRINKING LEVELS? COUPLE-DYAD MODELING OF NATIONAL GUARD SERVICE MEMBERS AND THEIR PARTNERS.

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Aims: Studies among military families suggest that National Guard service members and their family members engage in hazardous drinking ("alcohol consumption which confers the risk of physical and/or psychological harm") post deployment, especially when post-traumatic stress disorder (PTSD) is present in the family. Few studies have examined relative individual and couple PTSD effects; gender role may further complicate post deployment experience in the family. We chose heterosexual couples where one or both members had recently returned from deployment to examine the role of self and partner's PTSD on alcohol use and whether gender moderates the strength of this relationship.
Methods: Service members and their partners attending a National Guard reintegration event were recruited to participate in an in-depth telephone interview at approximately 2-4 months post deployment. Only dyad couples are included (n=156 couples) and were separately interviewed. The outcome measure is sum of Alcohol use disorder identification test items (AUDIT). Predictors of interest are high PTSD checklist score (>= 45) for self and partner, gender and recent deployment. We used multilevel modeling for dyads, and hierarchical techniques to account for effects of age, race, education, employment, parenthood, negative childhood events and additional predictors in stepwise models.
Results: Our preliminary results suggest that individuals and partner's drinking levels were significantly correlated. Although, overall men were drinking more than women, this pattern was reversed when introducing dyadic and individual confounders. PTSD is significantly associated with alcohol use levels only among those deployed, as expected; Women, not men, had increased drinking levels with PTSD ($b=-4.11$, $p < .01$), reaching closer to men's drinking levels.
Conclusions: Individual's own PTSD levels affected drinking, relative to partner's effects with no evidence for cross-dyad effect. Women with PTSD had higher drinking levels than those without PTSD.
Financial Support: NIDA T32DA007313; DoD W81XWU1120108

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EFFECTS OF CHILDHOOD TRAUMA ON PSYCHOPATHOLOGY, RISKY SEX, AGGRESSION, AND EMOTION DYSREGULATION AMONG INPATIENT SUBSTANCE USERS.

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Aims: Elevated rates of childhood abuse are reported by adults with substance use disorders (SUDs). Research among youth has demonstrated that specific types of abuse lead to particular negative outcomes; it is not known whether this pattern holds for adults with SUDs. We hypothesized that more generally, childhood abuse would lead to psychopathology and more specifically, sexual abuse (SA) would lead to risky sex, physical abuse (PA) would lead to aggressive behaviors, and emotional abuse (EA) would lead to emotion dysregulation in substance users.
Methods: 280 inpatients in substance use treatment completed the Structured Clinical Interview for the DSM-IV, the Childhood Trauma Questionnaire (CTQ), the HIV Risk-Taking Behavior Scale, a legal status questionnaire, the Difficulties with Emotion Regulation Scale (DERS), and the Distress Tolerance Scale (DTS).
Results: Using regression, higher scores on the CTQ were associated with elevated rates of psychiatric and SUDs ($\beta=.387$, $t(268)=6.83$, $p<.001$). The CTQ Sexual Abuse subscale predicted exchanging sex for cocaine ($\beta=.218$, $t(259)=2.68$, $p=.008$) and for heroin ($\beta=.317$, $t(259)=2.27$, $p=.026$); PA, and EA were non-significant (NS) predictors. The Sexual Abuse subscale predicted number of arrests for prostitution ($\beta=.212$, $t(272)=2.87$, $p=.004$), engaging in unprotected sex with a casual partner ($\beta=.156$, $t(272)=2.06$, $p=.041$), and experiencing low sexual arousal when sober ($\beta=-.151$, $t(268)=-2.06$, $p=.041$); PA and EA were NS predictors. The Physical Abuse subscale predicted number of arrests and charges for assault ($\beta=.324$, $t(268)=3.57$, $p<.001$), and weapons offenses ($\beta=.274$, $t(268)=3.06$, $p=.002$); EA and SA were NS predictors. The Emotional Abuse subscale predicted the DERS total ($\beta=.614$, $t(272)=3.90$, $p<.001$) and predicted lower levels of distress tolerance on the DTS ($\beta=-.461$, $t(272)=-2.69$, $p=.009$); PA and SA were NS predictors.
Conclusions: Different types of childhood abuse lead to particular negative outcomes in adulthood among substance users.
Financial Support: This work was supported in part by NIDA grant R01 DA19405
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TRAJECTORIES OF DAILY CIGARETTE USE FROM MID-ADOLESCENCE TO YOUNG ADULTHOOD: THE ROLE OF DEPRESSIVE SYMPTOMS.

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Aims: During adolescence both depressive symptoms and cigarette use are found to increase rapidly. Further, depressive symptoms have long been suggested to play a role in the onset and establishment of smoking. To date, however, whether depressive symptoms influence daily cigarette use differently for different kinds of adolescent smokers has not been established. The aim of this study is to examine if depressive symptoms influence the smoking trajectories of individual smokers followed from mid-adolescence to young adulthood.
Methods: Participants (n=3,290) came from the National Longitudinal Study of Adolescent Health who were assessed at four time points. The first wave included adolescents who were between 10-19 years of age and they were re-contacted 4 times; at the most recent assessment participants were 22-31 years of age. The analytic sample included participants (mean age at Wave 1=16.01, 48% female) who reported smoking at each of the four time points. Latent class growth mixture modeling determined membership in latent classes of daily cigarette use assessed longitudinally.
Results: A 3-class solution was selected, based on the BIC and the bootstrapped likelihood ratio test. The three classes were named Heavy continuous users (11%), Late-starting users (0.6%), and Occasional users (88%). Further, regression analyses examined whether depressive symptoms predicted class membership. Depressive symptoms, as assessed by the CES-D, at the initial wave were found to differentially predict class membership for the Late-starting smokers, but not for the other two classes.
Conclusions: The results of the present longitudinal study suggest that most smokers in this nationally representative sample of adolescents who were followed into early adulthood are characterized as being occasional users. Further, we found that depressive symptoms influence the group of adolescents who steadily increase the number of cigarettes smoked per day in early adulthood. The findings have implications for coordinated mental health and substance use treatment.
Financial Support: No financial support was received.

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ADAPTATION OF THE HIPPOCAMPUS-ACCUMBENS PATHWAY FOLLOWING REPEATED COCAINE.

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Aims: Dopaminergic (DA) neurotransmission in the nucleus accumbens (NAc) is important for various cognitive processes including reinforcement learning. Phasic elevations of DA the NAc evoked by unconditioned stimuli are dependent on impulse flow from the ventral hippocampus. Repeated cocaine exposure is associated with a strengthening of hippocampal synaptic plasticity. Therefore, augmentation of hippocampal output may be one mechanism by which drugs of abuse enhance limbic dopamine activity. In the present study we investigated the effect of repeated cocaine on the pathway between the ventral hippocampus and the medial shell of the NAc.
Methods: The day following the last of seven daily injections of saline or cocaine (20 mg/kg, ip.), in vivo microdialysis in freely moving adult male Sprague-Dawley rats was performed. In addition, since immature neurons in the hippocampus are more excitable than mature neurons, and repeated cocaine increases markers of immature neurons in the dentate gyrus of the hippocampus, the effect of repeated cocaine on immature (doublecortin-immunopositive) neurons is under investigation.
Results: Unilateral infusion of NMDA (0.5μg) into the ventral hippocampus produced a transient increase in both behavioral activity and ipsilateral DA efflux in the medial shell of the NAc.
Preliminary evidence indicates that NMDA-induced increases in behavioral activity and DA efflux are enhanced in rats that previously received repeated cocaine.
Conclusions: Facilitated ventral hippocampal–NAc communication following repeated cocaine may underlie enhanced cue-evoked dopaminergic neurotransmission that promotes reward-seeking behavior and increased behavioral responses to psychostimulants
Financial Support: T32 DA07237, P30 DA13429, R01 DA018326

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PREVALENCE OF PSYCHIATRIC DISORDERS AMONG TREATMENT-SEEKING INDIVIDUALS WITH CO-OCCURRING CHRONIC PAIN AND OPIOID DEPENDENCE.

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Aims: This study explored the prevalence of DSM-IV (APA, 1994) current and lifetime Axis I and current Axis II psychiatric disorders among individuals seeking treatment for co-occurring chronic pain and opioid dependence (POD).
Methods: 134 consecutive adults seeking opioid agonist maintenance treatment were evaluated by masters- or doctoral-level research clinicians using the Structured Clinical Interview for DSM-IV Axis I Disorders and the Diagnostic Interview for DSM-IV Personality Disorders.
Results: Participants ranged in age from 20 to 64 years old (M = 36.3, SD = 10.2); 90 (68%) were men; 118 (89%) were white. Prevalence of current and lifetime disorders were as follows: mood (50% and 55%), anxiety (48% and 53%), and non-opioid substance use disorders (45% and 73%). Major depression was the most prevalent current and lifetime mood disorder (36% and 47%), while PTSD (24% and 26%) and panic disorder (21% and 21%) were the most prevalent current and lifetime anxiety disorders. Current and lifetime non-opioid substance use disorders were common, including abuse or dependence on: alcohol (9% and 54%), cannabis (15% and 36%), and cocaine (18% and 41%). A plurality of patients met criteria for any Axis II disorder (56%); the most frequently occurring personality disorders were: antisocial (20%), avoidant (19%), paranoid (16%), borderline (13%), and obsessive compulsive (13%).
Conclusions: While chronic pain and opioid dependence are each associated with increased prevalence of co-occurring psychiatric disorders (compared to the general population), the combination of the two in the form of POD appears to have an additive effect, and supports the need for clinicians to assess and address these comorbid psychiatric conditions among individuals with POD seeking opioid agonist maintenance treatment.
Financial Support: NIDA (K23 DA024050, K24 DA00445)

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LOW INCIDENCE OF CARDIAC DIAGNOSES IN METHADONE PATIENTS: NO ASSOCIATION WITH QTC.

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Aims: Methadone is associated with prolongation of the cardiac QTc interval. Prolongation of the QTc interval may be associated with increased risk for sudden cardiac death (SCD). A recent report from the Substance Abuse and Mental Health Services Administration recommends a risk mitigation approach for SCD in methadone maintained patients. There is little information, however, about the incidence of cardiac arrhythmia or SCD in methadone patients.
Methods: We queried an electronic health record (EHR) for any diagnosis of a cardiac conduction disorder (ICD-9 group 426) or cardiac dysrhythmia (ICD-9 group 427) in 749 methadone maintained patients who had at least one ECG result within the EHR. Incidences of ICD-9 diagnoses were calculated per 10,000 patient years. Chi-square and t-tests were used to compare patient demographics and QTc intervals between those with ICD-9 diagnoses made when they were on methadone (ON) and those with ICD-9 diagnoses made when they were off methadone (OFF).
Results: Of 749 patients, 346 had at least one ECG ON and 403 OFF. Compared to patients OFF, those ON were older, more likely to have a QTc >500 msec, and had longer mean QTc (439 msec v 423 msec). Thirty-five of 749 patients received at least one ICD-9 group 426 or 427 diagnosis, 23 ON and 12 OFF. There was no difference in diagnoses between groups. Of diagnoses associated with risk for SCD the most common were sinus bradycardia (12), cardiac arrest (3), long QT syndrome (2), and ventricular tachycardia (2). Chart review revealed misclassification of both long QT syndrome diagnoses. Diagnoses occurred in 14/10,000 and 10.6/10,000 patient years for those ON and OFF, respectively (p>0.1). QTc did not differ between those receiving ICD-9 diagnosis ON versus OFF.
Conclusions: EHR review of more than 6,600 methadone patient years found that while methadone is associated with prolongation of the QTc interval, the incidence of diagnoses associated with risk for SCD is low and not related to the QTc interval.
Financial Support: NIDA K23DA024663

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EFFECTIVENESS OF THE TREATMENT RETENTION AND INDUCTION PROGRAM (TRIP) FOR INCREASING ADOLESCENT MOTIVATION FOR CHANGE.

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Aims: Success in substance abuse treatment requires recognition that there is a problem, desire to seek help, and readiness to engage in treatment. Interventions that incorporate cognitive techniques, such as the TRIP, may serve as an enhanced motivational tool beyond standard care. The purpose of this study is to determine the effectiveness of TRIP on treatment motivation. Compared to Standard Practice, clients who get TRIP plus Standard Practice are expected to have greater recognition of personal problems and treatment needs at Time 2. Furthermore, gains are expected to depend upon level of impulsivity at Time 1. In accordance with Prochaska and DiClemente's (1986) Stages of Change, TRIP may affect desire for help (DH) and treatment readiness (TR; later stages of change) through the association with changes in problem recognition (PR; an early stage of change).
Methods: Data were collected in 2011 and 2012, as a part of the TCU Adolescent Project and represent 506 clients from 6 residential facilities that completed assessments at intake (Time 1) and at 35 days (Time 2). Half of the sample (n = 251) enrolled in treatment prior to facility implementation of TRIP (Standard Practice Group); 255 clients entered treatment after TRIP implementation began and received Standard Practice enhanced by TRIP. Multiple regressions were conducted with each of the motivation scales as dependent measures at Time 2, controlling for motivation at Time 1.
Results: Analyses suggest that adolescents involved in TRIP report greater PR and treatment needs at Time 2 than those who did not receive TRIP. No treatment effects were found on DH or TR. Highly impulsive clients report greater PR, but lower DH and TR.
Conclusions: Findings suggest that participation in TRIP results in higher ratings on early stages of the individual change process; however, later stages of change do not appear to be directly affected by TRIP. Research is needed to identify the core components of TRIP that affect problem recognition and treatment needs among adolescents in treatment.
Financial Support: NIDA grant R01DA013093.

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FEASIBILITY, ACCEPTABILITY, AND INITIAL EFFICACY OF PAIN MANAGEMENT GROUPS IN METHADONE MAINTENANCE TREATMENT.

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Aims: Despite calls for improved pain management in methadone maintenance treatment (MMT), few studies have investigated the use of nonpharmacological pain interventions in this setting. We examined the feasibility, acceptability, and initial efficacy of four MMT groups for pain that were based on a cognitive-behavioral therapy model: Coping with Pain (CWP), Relaxation Training (RT), Music Group (MG), and Mindful Walking (MW).
Methods: We posted advertisements for the four open groups at a MMT clinic with a census of approximately 900 patients. Brief pre- and post-session standardized questionnaires were administered to group attendees. Data Analysis: We employed analysis of variance and chi-square data analytic strategies.
Results: 343 patients (53% male, 51% white) attended at least one of the four types of groups. Mean satisfaction (scored on 1-6 Likert-type scale) was similarly high across CWP (4.6), RT (4.7), MG (4.9), and MW (4.3). The repeat session attendance rate was higher ($p<.05$) among individuals in CWP (43%), RT (43%), and MG (40%) than those in MW (14%). Repeat attendance was associated ($p<.05$) with reductions in worst, typical, current, and characteristic pain intensity; depression; and emotional distress due to pain (CWP); anxiety (RT); and pain interference (MG). Repeat attendees at RT also reported increased time spent per week doing relaxing activities ($p<.05$).
Conclusions: Group MMT interventions for pain management seem feasible and acceptable. Repeat attendance at groups may be associated with differential reductions in pain or psychiatric symptoms, depending on the group type.
Financial Support: NIDA (K23 DA024050, K24 DA00445)

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WITHDRAWN

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ALCOHOL DEMAND INDICES PREDICT OUTCOMES AMONG HEAVY-DRINKING YOUNG ADULTS RECEIVING A BRIEF INTERVENTION.

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Aims: This study looked at the impact of baseline alcohol demand indices on alcohol consumption following a brief alcohol intervention.
Methods: Participants (N=150, 43% female, 65% White, ages 17 to 20) were non-college-attending heavy episodic drinkers proactively enrolled in an intervention study that compared the efficacy of a motivational interview (MI) and relaxation training control (REL) on reducing alcohol use. Using self-reported data, we calculated participants' average number of drinks per week and frequency of heavy drinking (HD, 5+ drinks) at baseline, a 6 week follow up (W6), and a three month (M3) follow up. At baseline, participants also completed a hypothetical alcohol purchase task, by indicating how many alcoholic drinks they would purchase and consume across a range of prices ($0 to $20). From this task, five demand indices were calculated: Breakpoint (first price that completely suppresses consumption), Omax (maximum expenditure), Pmax (price at which demand become elastic), Intensity (consumption when drinks are free), and elasticity (slope of the demand curve, or sensitivity to price).
Results: Hierarchical regressions controlling for gender and baseline drinking showed that several demand indices were predictive of drinking outcomes. Specifically, greater baseline Omax and intensity, and less elasticity predicted more W6 drinks/week in the MI condition. At M3, greater baseline breakpoint, Omax, intensity, and less elasticity predicted more drinks/week in the REL condition. Demand indices were predictive of W6 HD frequency in the MI condition and M3 HD frequency in the REL condition.
Conclusions: The results suggest that elevated demand indices (except elasticity, which negatively predicted consumption) may be a risk factor of poor intervention response. However, there were differences according to condition, assessment period, and alcohol use measures.
Financial Support: The first author plans to complete the early career travel award application. Otherwise, there is currently no support.

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PAIR HOUSING OF JUVENILE MALE RHESUS MACAQUES: A PILOT STUDY.

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Aims: Current regulations are based on the assumption that social housing may be beneficial for nonhuman primates used in research that live in groups in their natural habitat. However, evidence supporting this assumption is limited. Moreover, the possible impact of social housing and subsequent separation on studies of abused drugs is unknown. Subordinate status and separation during social housing have each been shown to increase drug self-administration.
Methods: To begin to address these questions, we paired 6 experimentally-naïve juvenile (aged 3.15±0.33 years) male rhesus macaques based on observations of aggressive, fearful, or neutral behaviors while individually housed. Animals were introduced to pair housing in three stages: protected contact, grooming contact, and ultimately full contact. Each pair progressed through all stages and no serious injury requiring separation occurred. Five-minute behavioral assessments were conducted by trained observers who recorded the frequency and duration of behaviors on a standardized form. Observations were made 3 times a day at the beginning of each phase.
Results: Comparison of behaviors in these animals before and during social housing revealed very low levels of stereotypy and anxiety-like behavior, such as pacing, yawning and vigilant scanning. However, the frequency of stereotypy was decreased further at the full contact phase relative to the individual housing stage. Aggressive and affiliative behaviors were increased immediately following full access, but aggressive behavior decreased with time while affiliative behavior persisted. Interestingly, aggression toward the observers during individual housing did not predict dominant status (evidenced by greater mounting) within the pair.
Conclusions: A critical question that remains to be resolved is whether social housing and separation will affect the response to drugs of abuse once these animals enter operant behavioral studies.
Financial Support: Supported by DA002519, DA024642, and DA007252.

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NEURAL CORRELATES OF CROSS-COMMODITY DISCOUNTING IN COCAINE USERS AND CONTROLS.

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Aims: Cocaine users (CU) discount delayed monetary reinforcers to a greater extent than control participants (CP). In a prior study of cross-commodity discounting of cocaine and money in CUs, we showed that discount rate depended upon both the commodity and its temporal location. Here we compare chronic cocaine users vs. community controls on the behavior and brain activity from single and cross-commodity discounting for cocaine and money.
Methods: Participants chose between hypothetical quantities of money now vs. money later (M-M), cocaine now vs. cocaine later (C-C), money now vs. cocaine later (M-C), and cocaine now vs. money later (C-M) in a fMRI scanner. Indifference points and neural response were obtained.
Results: Single-Commodity. Consistent with prior research, CUs (M±SEM) discounted M-M significantly more than CP ($p<.01$). Group comparisons showed that during M-M, CPs had greater activity than CUs in the sup. parietal lobe, post. cingulate, insula and mid. frontal cortex, consistent with the behavior results. Interestingly, whole brain analysis (vox $p<.01$, etv 15, unc) revealed that during C-C, CPs had greater activity than CUs in the post. cingulate, amygdala, striatum, insula and mPFC, suggesting greater neural involvement when making choices for a substance they have never used.
Cross-Commodity. During M-C, CPs had greater activity than CUs in the sup. parietal lobe, temporal lobe, posterior cingulate and sup. frontal lobe. During C-M, however, CUs had greater activity than CPs in the striatum, orbital frontal cortex and mPFC. Finally, CUs had greater activity in the striatum, rostral PFC and inf. PFC during C-M than M-M, M-C and C-C
Conclusions: We show that devaluing future rewards in cocaine users is greatest when cocaine is the immediately available reinforcer. Furthermore, cross-commodity devaluing in cocaine users involves the allocation of functional resources towards choosing the presently available cocaine option.
Financial Support: Supported by NIDA DA040241

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A MIXED KAPPA/MU PARTIAL OPIOID AGONIST ATTENUATED COCAINE-INDUCED LOCOMOTION.

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Aims: The purpose of this study was to evaluate an aminothiazolomorphinan, MCL-420, with partial agonist properties at mu and kappa opioid receptors to determine if it would reduce cocaine-induced locomotor activity in mice.
Methods: ICR mice were acclimated to the open field chamber for 30 min before vehicle or MCL-420 administration. Locomotor activity was measured in an Open Field Locomotor System with 16 light beams. MCL-420 was tested alone and in the presence of cocaine (20 mg/kg, i.p.). The number of ambulations over 120 min was recorded.
Results: MCL-420 at doses of 1 and 10 mg/kg did not have any effect on the number of ambulations per min in comparison to vehicle-treated controls. A dose of 30 mg/kg of MCL-420 produced a slight increase in the number of ambulations per min. MCL-420 at doses of 10 and 30 mg/kg reduced the cocaine-induced increase in the number of ambulations.
Conclusions: MCL-420 partially reduced cocaine-induced loconotor activity in a dose-dependent manner. The kappa/mu partial agonist properties of MCL-420 may account for it ability to partially suppress cocaine-induced locomotor activity.
Financial Support: NIDA grant DA014521 and Paul Stark Endowed Professorship.

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TRENDS IN OVERDOSE DEATHS AFTER RELEASE FROM STATE PRISON, 1999-2009.

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Aims: Studies have demonstrated a high risk of death among former prison inmates, particularly from drug-related causes. We sought to assess trends in mortality due to all-cause and unintentional poisoning (overdose) among former inmates released between 1999 and 2009.
Methods: We conducted a retrospective cohort study of 76,208 inmates released from Washington state prisons (192,511 releases). Identities were linked probabilistically to the National Death Index to identify deaths. Incidence mortality rates (IMR, deaths per 100,000 person-years [p-y] of risk) were calculated for all-cause, unintentional injuries, unintentional poisoning, and opioid-related deaths. We computed standard mortality ratios (SMR) and 95% confidence intervals (CI) to compare IMRs to the non-institutionalized population, using data from CDC Wonder and adjusting for age, gender and race.
Results: There were 2,462 deaths during 334,263 p-y after release from prison. The all-cause mortality rate (IMR) was 737/100,000 p-y. Among the major categories of death, the highest mortality rate was due to unintentional injuries (828 deaths; IMR 248/100,000 p-y) and occurred at a mean age of 40. Of these, 558 deaths were due to unintentional poisoning (IMR 167/100,000 p-y). Among all causes, opioids were involved in 315 deaths (IMR 94/100,000 p-y). Released inmates had a higher mortality rate than non-institutionalized Washingtonians from all causes (SMR 3.6, 95% CI 3.5, 3.7) and unintentional injuries (SMR 5.9, 95% CI 5.6, 6.3). Whereas all-cause mortality rates were higher among men than women (IMR 752 vs. 653/100,000 p-y), unintentional poisoning mortality rates were lower among men (IMR 154 vs. 236/100,000 p-y).
Conclusions: Our results demonstrate a persistent burden of overdose death after release from prison. To reduce the risk of overdose, it is critical to increase collaboration between criminal justice and community health and substance abuse service agencies to test and implement in-prison and post-release interventions after release from prison.
Financial Support: National Institute on Drug Abuse DA031041

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CHANGING PATTERNS OF ONSET OF NONMEDICAL PRESCRIPTION OPIOID USE RELATIVE TO OTHER DRUGS FROM ADOLESCENCE TO EARLY ADULTHOOD.

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Aims: Although adolescence is the period of highest risk of initiating nonmedical prescription (NMP) opioid use and there is a high prevalence of other drug use among NMP opioid users, little is known about patterns of onset of opioids and other drugs through this developmental stage. This study examines the relative prevalence and age of onset of opioids and other drugs within a cohort of adolescents using multiple cross-sectional surveys of the National Survey on Drug Use and Health (NSDUH).
Methods: Data from the 2002-2010 NSDUH were used to track drug use in a cohort from age 12-13 to 20-21 (ie, 12-13 year olds (yo) in the 2002 NSDUH, 14-15 yo in 2004, 16-17 yo in 2006, 18-19 yo in 2008, and 20-21 yo in 2010). The prevalence of lifetime and past-year drug use was assessed at each age, as well as the age of onset of opioids and other drugs.
Results: At age 12-13 yo, lifetime prevalence of marijuana and NMP opioid use were equal (4%) but increased more rapidly for marijuana, reaching 52% by age 20-21 versus 23% for NMP opioid use. Among the 4% who used opioids by 12-13 yo, 18% had started marijuana use; this increases to 50% and 85% among those who start NMP opioid use by age 14-15 and 20-21 yo, respectively. Among those using opioids by 20-21 yo, 63% initiated marijuana use prior to opioids, 13% started use of both drugs at the same age, 9% started marijuana after opioids, and 15% never used marijuana. In contrast, 8% and 25% of those who started NMP opioid use by age 12-13 and 14-15, respectively, had used marijuana prior to opioids. Regardless of age of opioid initiation, alcohol and tobacco use tended to precede opioids and cocaine and heroin to come after opioids..
Conclusions: By early adulthood (20-21 yo), most who started NMP opioid use had already started use of marijuana, but opioid use tended to precede marijuana use in early adolescence (12-15 years). These findings point to changing patterns of onset across developmental stages that should be addressed in prevention and intervention strategies.
Financial Support: Funded by Purdue Pharma, L.P.

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FINANCIAL CAPABILITY: STANDARDIZING ASSESSMENT FOR ADULT BENEFICIARIES WITH CO-OCCURRING DISORDERS.

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Aims: In 2011, 6.5 million adults with psychiatric disorders received Social Security benefits to provide for basic needs. Payments typically made directly to the beneficiary may be assigned to a representative payee if the beneficiary is determined not capable to manage funds. SSA assesses capability as "the ability to understand and act on the ordinary affairs of life, such as providing for own adequate food, housing, clothing, etc., and the ability, in spite of physical impairments, to manage funds or direct others how to manage them" (SSA, 2010). The breadth of the current definition poses the risk that bias and subjectivity may influence conclusions on this high-stakes assessment. The aim of this study was to develop an instrument to further standardize clinician assessment of financial capability for adults with co-occurring disorders.
Methods: A 58-item questionnaire was pilot-tested with clinicians of 122 adult beneficiaries with substance abuse/dependence receiving intensive psychiatric care. Items were based on expert consensus about manifestations, correlates, and consequences of financial incapability. Data analyses explored response distributions, tested factorial validity, item reliability, and compared assessment-based capability determinations to gold-standard findings. Items were trimmed based on a priori item function criteria.
Results: Clinicians lacked specific information about patients' financial management; "don't know" responses created high rates of missing data. Items involving gambling problems generally were not endorsed. One-week test-retest reliability ranged from r=.18-.98; item-total correlations were r=.06-.85. CFA-confirmed subscales of spending on non-essentials, failing to meet basic needs, spending on harmful things, and future likelihood of misspending led to capability determinations that matched the gold standard for 75% of cases.
Conclusions: The questionnaire was reduced to 27 most salient and reliable items. The next phase will validate the reduced questionnaire.
Financial Support: NIDA; 1R01DA025613 (M.I. Rosen)

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CHRONIC METHAMPHETAMINE USE HEIGHTENS CONCURRENT RISK OF FUNCTIONAL DEPENDENCE IN PERSONS LIVING WITH HIV INFECTION.

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Aims: Disability among chronic methamphetamine (MA) users is multifactorial. We examined the additive adverse impact of HIV infection, a common comorbidity in MA users, on functional dependence.
Methods: Participants (N=798) were stratified by lifetime MA dependence diagnoses (ie,MA+ or MA-) and HIV serostatus (ie,HIV+ or HIV-) and underwent comprehensive neuromedical, neuropsychiatric, and functional research evaluations, including assessment of neurocognitive symptoms in daily life, instrumental and basic activities of daily living, and employment status.
Results: A logistic regression revealed additive effects of HIV and MA across all measures of functional dependence, independent of other demographic, psychiatric, and substance use factors. The prevalence of global functional dependence increased in the expected stepwise fashion, with the lowest rates in the HIV-/MA- group (29%) and the highest rates in the HIV+/MA+ sample (69%). Post-hoc ANOVAs indicated that the impact of HIV on MA-associated functional dependence was moderated by nadir CD4 (ie,historic immunosuppression), such that MA use was associated with greater disability among HIV+ persons with higher, but not lower nadir CD4. A logistic regression within the HIV+/MA+ cohort illustrated that functional dependence was reliably associated with neurocognitive impairment, lower cognitive reserve, polysubstance use, and major depressive disorder.
Conclusions: HIV infection confers an increased risk of MA-associated disability, particularly among HIV+ persons without histories of immune compromise. Standard MA treatment approaches may benefit from compensatory strategies aimed at counteracting the effects of low cognitive reserve, neurocognitive impairment, and psychiatric comorbidities for functional dependence in the context of HIV.
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FACTORS ASSOCIATED WITH TIME TO INJECTION INITIATION AMONG DRUG INJECTORS.

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Aims: Few studies have examined time to injection (TIJ) initiation (years from first illicit drug use to first injection). Our aims are to calculate TIJ and to examine factors associated with TIJ in a sample of drug injectors.
Methods: As part of an exploratory study on injection drug initiation, interviews were conducted with drug injectors recruited at outreach sites in Los Angeles and San Francisco, CA (n=549) during 2011-12. Interviews covered demographics, family history, drug use and drug injection initiation among others. TIJ was calculated by subtracting age at first drug injection from age of first illicit drug use. We used multivariate linear regression to determine factors independently associated with TIJ.
Results: The sample was 33% White, 32% Black, 25% Latino, 27% female, and 60% homeless. Mean age was 46.9 (IQR 41, 56) and mean years of drug injection were 24.8 (IQR 13, 36). Mean age of first illicit drug use was 13.8 (IQR 12, 15) and mean age of injection initiation was 22.1 (IQR 16, 26). Mean TIJ for the sample was 8.4 (IQR 2, 12) years. In a multivariate linear regression model, we found that drug types ever used were associated with TIJ (crack use= +2.9 years, p=0.004; powder cocaine use=+3.3 years, p<0.001; heroin use=-3.2 years, p=0.009; prescription stimulants use= -2.6 years, p=0.001). Any substance abuse treatment prior to injection was associated with longer TIJ (+3.9 years, p<0.001), while being born after 1979 (-2.9, p=003) and having your first injection administered by a family member (-3.4 years, p=0.006) or self (-2.1 years, p=0.016) were associated with shorter TIJ.
Conclusions: TIJ was influenced by drug type, substance abuse treatment, birth cohort, and injection initiator characteristics. These data highlight the need for surveillance of emerging trends in injection drug use and novel prevention strategies targeting transitions to injection among at-risk populations.
Financial Support: NIDA grant number R01DA027689 and R01DA030427.

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OVERDOSE EXPERIENCES AMONG PATIENTS AT AN URBAN EMERGENCY DEPARTMENT.

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Aims: While it is known that emergency department (ED) patients have elevated levels of substance use, little research has examined their overdose histories. The purpose of this study was to describe overdose experiences among ED patients and examine substance use correlates of overdose history.
Methods: A random sample (n=3,696) of patients waiting for care at an urban ED in Flint, Michigan, were approach between February 2011 and August 2012 and recruited to participate in a computerized self-assessment. Multivariable logistic regression was used to examine the association of patient characteristics with lifetime overdose history.
Results: 450 (12.2%) respondents reported one or more overdoses in their lifetime. In an adjusted model, past year non-medical prescription opioid use (odds ratio [OR] = 3.6, 95% Confidence Interval [CI]: 2.4-5.5), non-medical prescription sedative use (OR = 2.7, 95% CI: 2.4-4.4), cocaine use (OR = 2.4, 95% CI: 1.6-2.7), marijuana use (OR = 1.6, 95% CI: 1.2-2.0), and binge drinking on a monthly basis or more (OR = 2.1; 95% CI: 1.6-2.7) were independently associated with overdose history. In a separate adjusted model, use of any one drug compared to none was associated with an OR of 1.3 (95% CI: 1.0-1.8), two drugs compared to none was associated with an OR of 2.5 (95% CI: 1.9-3.4), three drugs compared to none was associated with an OR of 4.4 (95% CI: 3.0-6.5), and four or more drugs compared to none was associated with an OR of 13.8 (95% CI: 8.5-22.4).
Conclusions: Overdose was relatively common among ED patients. Individuals who use multiple drugs are more likely to have had an overdose. Given that prior overdose is the strongest predictor of future overdose, these findings can inform screening methods to identify ED patients at risk for future overdoses.
Financial Support: Funding was received from NIH grant R01DA026029 and VA grant CDA-09-204.

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TOBACCO USE DISORDER AND THE RISK OF COMPLETED SUICIDE IN VHA.

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Aims: The few studies that have examined the relationship between tobacco use and completed suicide have generally found that current tobacco use confers an increased risk of suicide. Nonetheless, this prior research has been limited by relatively small sample sizes, and incomplete statistical adjustment, especially with respect to co-occurring psychiatric illness. Therefore, we estimate the hypothesized link between tobacco use disorder (TUD) and suicide using data from a large health system, adjusting for important confounding variables.
Methods: Data for this study included all users who received Veterans Health Administration (VHA) services in Fiscal Year (FY)2005 and were alive at the start of FY2006 (n=4,863,086). The cohort was followed FY2006-2008 for the outcome of completed suicide, as assessed via National Death Index records. TUD was the focal independent variable of interest, and assessed via FY2004-2005 patient medical records. Cox proportional hazards regression models were performed to estimate the association between TUD and the risk of suicide during the follow-up interval. Unadjusted and adjusted models were estimated, with a fully adjusted model that included demographic variables, physical comorbidity, and psychiatric diagnoses.
Results: Of the 4,863,086 VHA users in the study, 4823 (0.1%) completed suicide during the follow-up interval. With adjustment for age, sex, and physical comorbidity, TUD was significantly associated with an increased risk of suicide (Hazard Ratio (HR)=1.8, 95% Confidence Interval (CI)=1.7, 1.9). When analyses also adjusted for co-occurring psychiatric conditions, the association between TUD and suicide death was moderately attenuated yet remained significant (HR=1.4, 95% CI=1.3, 1.5).
Conclusions: TUD may confer a small excess risk of death by suicide. Study results suggest that co-occurring psychiatric disorders may confound the relationship between TUD and suicide, and should be taken into account when studying the tobacco use-suicide relationship.
Financial Support: VA Office of Mental Health Services and Office of Mental Health Operations

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UNANTICIPATED CONSEQUENCES OF NON-DRUG-FOCUSED HIV PREVENTION INTERVENTION: CHANGES IN DRUG USE.

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Aims: To investigate whether longitudinal drug use declines after an HIV community prevention trial of sexual risk reduction (SR) intervention compared to a social services (SS) intervention in rural African-American (AA) non-IDU cocaine users in Arkansas.
Methods: Participants were recruited with Respondent-Driven Sampling in two rural majority African-American counties. The SR and SS conditions were matched for contact time and both were grounded in Social Cognitive Theory. Both included eight meetings (two small same-gender groups, two larger mixed-gender groups, and four individual sessions) over four months. Neither condition focused on drug use but both included information regarding risks associated with drug use. Follow-up interviews were at post-intervention, 6 and 12 months.
Results: 251 AAs (50% female, 50% high school graduate, mean age=38) were enrolled. Baseline substance use was 3.8 days powder cocaine use, 8.9 days crack, 15.3 days alcohol, 12.6 days marijuana in past 30 days) and did not differ significantly among conditions. Follow-up rates were 82%,76%, and 71%. Days of powder and crack cocaine, alcohol, and marijuana decreased significantly between baseline and post-intervention (1.6 days powder, 6.6 days crack, 12.9 days alcohol, 9.9 days marijuana) as did also ASI drug and alcohol composites; substance use or ASI did not change significantly between post and later interviews. Intervention condition was only significantly associated lower use of powder at 6 months. Women used more crack and powder over time (p=0.003), being employed was positively associated with substance use, and depression (PHQ-9) was significantly associated with greater ASI drug and alcohol composite scores.
Conclusions: Interventions to assist AA cocaine users with sexual risk and social services appear to also encourage lower substance use even though drug use was not explicitly targeted. Exploring the multi-directional associations among the changes in these risk behaviors in high-risk populations will be an important avenue for future research.
Financial Support: NIDA R01 DA024575

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ADOLESCENT INTERMITTENT ETHANOL EXPOSURE INCREASES RISKY RESPONDING IN A PROBABILITY DISCOUNTING TASK IN ADULTHOOD.

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Aims: Binge drinking during adolescence may alter risk-taking behavior in adulthood.
Methods: This study investigated the effects of adolescent intermittent ethanol (AIE) exposure on risk-taking in adulthood in Wistar rats. Adolescent (PND 28-53) rats received 5 g/kg of 25% (v/v) ethanol three times a day in a 2 days on/ 2 days off exposure pattern. In adulthood, risk-taking behavior was assessed in the probability discounting task under baseline conditions and after acute ethanol challenges (0, 1, 2, 3 g/kg).
Results: Under baseline conditions, when the large reward was delivered with high probability, all rats showed a preference for the large reward. When the large reward became unlikely, control rats became risk-averse, demonstrating a preference for the smaller, guaranteed reward. In contrast, AIE-exposed rats were risk-prone, continuing to prefer the risky alternative, even when large rewards were very unlikely. Acutely administered ethanol at all doses tested had no effect on risky choice and group differences were maintained, with AIE-exposed rats exhibiting more risky behavior than control rats. Nevertheless, the intermediate ethanol dose (2 g/kg) increased the number of trials required to complete the session in control, but not AIE-exposed rats, indicating some tolerance to the disruptive effect of ethanol in AIE-exposed rats. The highest ethanol dose tested (3 g/kg) increased the number of trials required to complete the session in both control and AIE-exposed rats, indicating that the high ethanol dose impaired performance in all rats. Notably, the observed performance deficits did not affect risk-taking in either the risk-averse control, or the risk-prone AIE-exposed rats.
Conclusions: Our results suggest that individuals exposed to ethanol binges during adolescence may take more risks as adults, compared to individuals without a history of adolescent binge drinking. Adolescent binge drinking may diminish ethanol-induced behavioral disruption without affecting risk taking during re-exposure to ethanol in adulthood.
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ADOLESCENT SUBSTANCE USE AND THE IDENTIFICATION OF SUBGROUPS.

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Aims: To identify subgroups of adolescents based on their past 12-months use of tobacco, alcohol, marijuana, illicit drugs, nonmedical use and excessive medical use of prescription medications.
Methods: A cross-sectional web-based survey of adolescents from two school districts in Southeastern Michigan was conducted. The sample was comprised of 2,744 middle-school (7th and 8th grade) and high-school (9th through 12th grade) students. Respondents had a mean age of 14.8 years (SD=1.9); 50.4% were female, 64.1% were Caucasian and 30.6% were African-American. Respondents completed measures of past 12-months substance use, parental monitoring, parental substance use, and internalizing and externalizing problems.
Results: Exploratory latent class analysis (LCA) indicated four classes. The largest class was comprised of respondents with low probabilities of using any substances (Low/No Use class), and the smallest class was comprised of respondents with relatively high probabilities of using all substances (Multiple Substances class). A third class included participants with high probabilities of using tobacco, alcohol, and marijuana (TAM). The fourth class consisted of participants with relatively high probabilities of using alcohol, nonmedical prescription medications, and excessive medical use of prescription medications (ANM). Parental monitoring, parental substance use problems, internalizing, and externalizing problems uniquely predicted membership in all three high-risk risk classes.
Conclusions: Results indicated three high-risk subgroups of adolescents, each characterized by a different pattern of substance use. Two risk groups are characterized by relatively high probabilities of prescription medication misuse.
Financial Support: This research was supported by research grants R01DA024678 and R01DA031160 from the National Institute on Drug Abuse, National Institutes of Health.

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INDIVIDUAL DIFFERENCES IN CONTROLLABILITY OF SOCIAL DEFEAT STRESS AS A PREDICTOR FOR ESCALATED COCAINE SELF-ADMINISTRATION.

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Aims: The small percentage of humans who experience traumatic events may become more vulnerable to later substance abuse disorder. Differences in response to social stress encounters were hypothesized to predict vulnerability to escalated cocaine taking.
Methods: Male Long-Evans rats were exposed to nine intermittent social defeat episodes over 21 days in an apparatus with three compartments permitting escape. To categorize individual subjects, we focused on the latency to enter a protective cage adjacent to the aggressor (threat zone), to escape from the aggressor after being defeated (fight), to return to the home cage (safe zone), as well as the total fight duration. For each behavior, individuals were rank-ordered based on these measures. Upon developing a behavioral profile for each individual, we then assessed saccharin preference, novelty-induced locomotion, cocaine-induced locomotion and intravenous cocaine taking. In a separate group of rats we measured total brain-derived neurotrophic factor (BDNF) and Trk-B receptor mRNA via RT-PCR in hippocampal tissue 1 hour after the last defeat.
Results: Those individuals consistently falling in the lower third of the ranks are characterized by fast active motor behaviors when entering the threat zone, escaping the fight and returning to the safe zone, as well as shorter fight durations. Importantly, these individuals were highly vulnerable to escalated cocaine taking during a 24-hour binge. Furthermore, there was a strong positive correlation between escalated cocaine intake and the probability to display a supine posture after an attack bite. Individuals consistently falling in the upper third of the ranks had a significantly blunted total BDNF and Trk-B mRNA in the hippocampus, suggesting a decreased sensitivity to social stress leading to suppressed cocaine taking.
Conclusions: These differences in controllability during threatening social encounters may provide a new basis for the development of behavioral profiling for appropriate therapeutic intervention in susceptible individuals.
Financial Support: NIDA DA 002632, 031734

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USER SATISFACTION WITH HEALTH CARE PROVIDED FOR ALCOHOL AND DRUG DEPENDENCY IN BRAZIL.

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Aims: The aim of the study was to measure patient satisfaction with health services providing treatment for alcohol and drug dependency in Brazil.
Methods: a cross-sectional study was performed between October 2011 and March 2012, in Brazil. A total of 1649 patients from alcohol and drug dependency health services were interviewed during the study period. Several aspects regarding client satisfaction were evaluated, including the patient view of knowledge, capacity and competence of health professional to listen and understand their problems.
Results: The patient response indicated, on average, a good satisfaction. The same results were observed when inquired about time to get an appointment, effect of the service in preventing relapses, and respect for individual rigths.
Conclusions: The results suggest that satisfaction seems to be present in the treatment processes, compliance, and positive outcomes of the studied services in Brazil. And, considering that they are inter-related, such results may be very helpful for health care evaluation in our setting. Also, responses to specific items are of interest to service providers who want to understand how a particular aspect of the service could be improved.
Financial Support: Grant from the Nacional Secretary of Alcohol and Drugs (SENAD), Brazil

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CHARACTERIZATION OF CHALLENGING EXPERIENCES (I.E., BAD TRIPS) AFTER INGESTING PSILOCYBIN.

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Aims: High-dose psilocybin sessions in supportive contexts have recently been reported to have sustained positive effects on attitudes, mood, and behavior. However, difficult experiences (i.e., 'bad trips,' which may include fear, anxiety, or paranoia) have been observed in some cases. The present analysis of high dose psilocybin sessions characterizes the incidence and predictors of having a bad trip and the correlation between bad trips and mystical experiences.
Methods: This analysis characterized bad trips from two previous studies (N= 54 participants at 30 mg/70kg psilocybin). Incidence of participant-rated fear, anxiety, and paranoia were examined using individual items (see below). Correlations were examined between participant post-session ratings of bad trips [the AIA (dread of ego dissolution) subscale of the APZ (an altered consciousness measure) and the sum of 10 'bad trip' items from the States of Consciousness Questionnaire (SOCQ) and Hallucinogen Rating Scale (HRS)] with demographics, personality measures, and a post-session measure of mystical experience.
Results: Participants rated strong or extreme "fear" (24%, 13/54) and anxiety ("trapped and helpless") (20%, 11/54); 17% (9/54) reported paranoia ("people... plotting against") at some point during the session. Younger participants had higher bad trip scores (AIA, $r = -.33$, $p < .05$; SOCQ/HRS, $r = -.27$, $p < .05$). AIA scores were significantly correlated with mystical experience scores ($r = .36$, $p < .01$).
Conclusions: Subjective-effects measures indicated substantial incidence of bad trip effects during high dose psilocybin sessions. Being younger seemed to increase risk for these experiences. However, such experiences were positively correlated with having a mystical experience. Further results from these experimental data and a survey of the general population will be reported at the conference.
Financial Support: NIDA grants R01DA03889 & T32DA007209, The Council on Spiritual Practices, The Heffter Research Institute

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MULTIPLE PROBLEM BEHAVIORS ASSOCIATED WITH AMPHETAMINE USE AMONG DELINQUENT AND INCARCERATED ADOLESCENTS IN LOS ANGELES COUNTY.

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Aims: Research has shown that problem behaviors such as substance use, delinquency and unplanned pregnancy often co-occur in adolescents and may be influenced by both independent and overlapping risk and protective factors rooted in personality, behavior and social context. Our purpose was to identify personality, behavior and social context factors specifically associated with amphetamine use in this population, for the purpose of informing preventive interventions and treatment.
Methods: Data was collected from 698 students aged 14 to 18 years attending alternative education and juvenile correction camp schools who participated in an HIV/STI prevention intervention. Multivariate regression and $\chi 2$ analyses using baseline data were used to explore associations of amphetamine use with other problem behaviors.
Results: Nearly 40% of the students reported lifetime amphetamine use (37%) whereas 17% had used amphetamines within the previous 90 days. Recent amphetamine use was highest among females (24%) and Latinos (22%) while very few African Americans reported recent use (<1%). Contextual predictors of amphetamine use included parental drug use and poor parental monitoring, whereas personality-related predictors included symptoms of anxiety. The hypothesis linking other problem behaviors to amphetamine use was supported by significant associations between amphetamine use and behavioral predictors such as other substance use, school expulsion, convictions for selling drugs and having made a partner pregnant (all $p < .05$).
Conclusions: The pervasiveness of associations with recent amphetamine use across personality, behavior and social context domains indicates the depth and complexity of this problem among delinquent adolescents. Interventions targeting delinquent and incarcerated adolescents would benefit from a holistic approach that addresses coping with difficult family environments and individual characteristics such as mood disorders while promoting substance use behavior change.
Financial Support: This research was supported by a National Institutes of Mental Health grant to Marguerita A. Lightfoot, Ph.D.

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13-YEAR OUTCOMES OF TREATMENT FOR METHAMPHETAMINE USE: PATTERNS OF USE AND CORRELATES.

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Aims: Evidence is accumulating on short-term effectiveness of treatment for methamphetamine (MA) use, but little is known about long-term outcomes. The study examines MA use for 13-years post-treatment, identifies use trajectories, and compares selected MA-user characteristics across pattern groups.
Methods: Data are from 3 successive Natural History Interviews for a sample of MA users randomly selected from mid-1990s treatment admission records in Los Angeles County. Interviews were conducted in 1999-2001 (n=351), 2001-03 (n=279), and 2009-12 (n=240) and included background, health, and risk behavior status and drug use, treatment, and criminal behavior histories over time. Monthly timelines were constructed for assessment of patterns of number of days per month with MA use. Group based trajectory analysis distinguished patterns across the post-treatment period. Pattern subgroups were compared on selected background, treatment, and post-treatment characteristics, using chi-square and general linear models.
Results: The sample was 44% female; 47% non-Hispanic white, 16% Black, 30% Hispanic, 6% other ethnicity. Of those with full follow-up, 15% were continuously MA-abstinent; an additional 65% were currently MA-abstinent but also had periods of use during follow-up. Five distinct post-treatment MA use patterns were identified: a continuously low/no use group (36% of sample), with 4 other groups with MA use directly following treatment but differing in timing of increase/decrease in use during follow-up. Few background characteristics distinguished the pattern groups. However, the low use group had highest rate of post-treatment self-help participation. Analysis will also compare the use pattern groups on current cognitive status, employment, and health characteristics.
Conclusions: Results illustrate the diverse post-treatment MA use patterns and support the need for continuing interventions for many users across an extended time following treatment. Further exploration of group differences may assist in identifying subgroups of MA users at most risk for continuing use and needing continuing care.
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SUBJECTIVE EFFECTS PRODUCED BY COCAINE ARE IN ASSOCIATION WITH GENETIC VARIANTS OF DAT1.

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Aims: The dopamine transporter (DAT) has been implicated in the subjective and reinforcing effects produced by cocaine, and polymorphisms within the DAT gene (DAT1, or SLC6A3) have also been linked to variations in the response to cocaine. The aim of the present study was to identify genetic markers of DAT1 that modulate subjective responses to cocaine in humans.
Methods: Non-treatment seeking, cocaine-dependent volunteers received a single bolus infusion of saline and cocaine (40 mg, IV). Subjective effects (visual analogue scales: VAS) were acquired before (-15 min) and up to 20 min after infusion. VAS scales ranged from zero (no effect) to 100 (greatest effect). Subjective effect values were normalized to baseline minus saline infusion values. Data was analyzed using repeated measures ANOVA. DNA from subjects was genotyped for the DAT1 intron 8 and 3′ UTR VNTRs.
Results: Cocaine-dependent participants (N=47) were ~44 years of age, black (68%) males (87%), who had ~13 years of education, and primarily smoked (94%) >2 grams of cocaine per day. Increased self-reports of "High" ($p = 2x10^{-4}$) and "Any Drug Effect" ($p = 5x10^{-5}$) were found to be in association with DAT1 (3′ UTR). The DAT1 intron 8 VNTR was also in association with increased self-reports of "Desire cocaine" ($p = 5x10^{-4}$), while the DAT1 3′ UTR VNTR was found to be in association with increased reports of "stimulated" ($p = 4x10^{-5}$).
Conclusions: The data presented here support the hypothesis that individual genetic differences within DAT1 contribute to variation within individual responses to cocaine among dependent individuals.
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A RCT OF LONG TERM RECOVERY MANAGEMENT (LTRM) FOR OPIOID OR STIMULANT DEPENDENCE.

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Aims: Evaluate the effectiveness of treatment as usual (TAU) vs. TAU + Long Term Recovery Management (LTRM), for adults seeking outpatient (OP) substance abuse treatment for stimulant or opioid dependence. It was hypothesized that LTRM participation would result in greater: reductions in drug use, retention in treatment, and exposure to 12-Step meetings.
Methods: This 12-month RCT had assessments at baseline, 6, and 12 months. A total of 203 adults enrolled in OP with primary opioid (n=143) or stimulant (n=60) dependence and were assigned to TAU (n=101) or LTRM (n=102). TAU received regular treatment at community treatment program sites. LTRM included 2 initial individual sessions, 1 group per month for 12 months, CM incentives for LTRM attendance, and re-engagement sessions.
Results: Sample was 67% male, 23% Black, 34 years old (mean). The LTRM group attended more OP sessions vs. TAU, 8.1 vs. 3.8 respectively ($p<0.01$). LTRM participants attended an average of 4.3 out of 14 LTRM sessions, 20 attended 0 sessions. Both groups significantly reduced substance use over 12 months. Randomization failed to make the groups equivalent at baseline with LTRM participants having more drug free days, weeks of abstinence, and self-help meetings attended. Adjusting for baseline differences, LTRM resulted in moderate-sized improvements in the proportion of drug free days from all drugs (effect size=13.9%, $p=0.16$, $d=0.28$) and self-help exposure (effect size=40.1 meetings, $p=0.01$, $d=0.52$).
Conclusions: LTRM is a promising approach for managing the chronic nature of addiction. While all participants significantly reduced drug use, LTRM significantly improved treatment and 12 Step meeting exposure. Future studies should focus on improving LTRM exposure and having greater power to detect meaningful differences in drug use outcomes.
Financial Support: NIDA:1RC1DA028467 (PI Carlson) & 1K23DA021512 (PI Brigham)

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THE EFFECTS OF TROPISETRON ON COCAINE-INDUCED CONDITIONED TASTE AVERSIONS.

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Aims: Cocaine, like other drugs of abuse, has both rewarding and aversive effects, and the balance of these effects may influence the drug's abuse potential. The conditioned taste aversion (CTA) preparation is an animal model used to assay the aversive effects of drugs. In this procedure, animals avoid consumption of a novel taste after it has been paired with a drug, a decrease in consumption indicative of the drug's aversive effects. The present study addressed whether pharmacological antagonism of 5-HT would result in attenuated cocaine-induced CTAs, indicating a role of 5-HT in cocaine's aversive effects. The specific 5-HT receptor, 5-HT3, was analyzed given that it is implicated in a variety of behavioral effects of cocaine.
Methods: This series of investigations first assessed the aversive effects of the 5-HT3 antagonist tropisetron alone (0, 0.056, 0.18 and 0.56 mg/kg) in the CTA design (Experiment 1). Following this, a non-aversion-inducing dose of tropisetron (0.18 mg/kg) was assessed for its ability to block aversions induced by a range of doss of cocaine (0, 10, 18, and 32 mg/kg; Experiment 2). Specifically, animals were given access to saccharin and then injected with various doses of cocaine (alone or in combination with tropisetron).
Results: Cocaine induced dose-dependent taste aversions that were not blocked by tropisetron. At the intermediate dose of cocaine, aversions were potentiated.
Conclusions: Tropisetron failed to attenuate cocaine-induced CTAs, suggesting that cocaine's aversive effects are not mediated by 5-HT, or at least this specific receptor subtype. The dose-dependent potentiation suggests that 5-HT may play a limiting role in cocaine's aversive effects.
Financial Support: Supported by a grant from the Mellon Foundation, the Mathias Research Award and American University's Scholars and Artists Fellowship.

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EVIDENCE-BASED MULTIMEDIA 12-STEP FACILITATION TOOLKIT IMPROVES COUNSELOR ADHERENCE IN GROUP COUNSELING WITH MINIMAL TRAINING: PRELIMINARY RESULTS.

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Aims: Numerous psychosocial interventions effectively improve client outcomes in clinical trials, but adapting evidence-based protocols into formats suitable for dissemination to community treatment programs is challenging. We translated 12-Step Facilitation (12SF) into a multimedia curriculum toolkit to help counselors deliver clinically useful group sessions that convey core elements of 12SF; we tested the toolkit's conceptual fidelity and clinical utility.
Methods: Toolkit material development was informed by consultation with content experts, counselors and clients, to develop simple, engaging presentations of core 12SF concepts. In a pre-post design, we coded 2 treatment groups on preselected 12-Step topics run by 10 counselors. Counselors were randomly assigned to attend a 3-hour training to familiarize them with the 12SF toolkit and accompanying self-teaching strategies (TK), or to an attention control training including relevant 12-Step content (AC). Post-training 12-Step groups were audiotaped and coded for adherence to 12-Step content and skillfulness. 12-Step engagement and self-reported substance use was assessed among clients (N = 44) for three months following toolkit exposure.
Results: TK counselors demonstrated very large and statistically significant Pre- to Post-Training adherence improvements in 12SF techniques (mean d = 1.74) and in 12-Step content (mean d = 1.49) relative to counselors in the AC condition. TK counselors also demonstrated moderate improvement in skill when delivering 12-Step content (mean d = 0.58). TK exposed clients self-reported significantly fewer drinking days (d = .59) and fewer drug use days (d = .49) relative to AC clients.
Conclusions: Preliminary results show that multimedia toolkits may be a cost-effective, easily disseminated approach to improve group counseling in community treatment with minimal training.
Financial Support: NIAAA R01 AA017867

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DISTINCT EXPRESSION PROFILES FOR CELL-SIGNALING MOLECULES IN MIDBRAIN DOPAMINE NEURONS FROM ANIMALS SHOWING RELAPSE VULNERABILITY TO COCAINE-SEEKING.

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Aims: Dysregulation of dopamine (DA) signaling is implicated in compulsive drug seeking. However, DA neuron molecular substrates that contribute to long-term relapse susceptibility remain to be fully elucidated. Potential substrates include brain derived neurotrophic factor (BDNF) and downstream signaling molecules. Therefore, we aimed to examine the expression of *BDNF* and other cell signaling transcripts within DA neurons isolated from animals characterised for relapse vulnerability. It was hypothesised that relapse-vulnerable animals would display distinct and lasting molecular changes compared to –resilient animals.
Methods: Using immuno-laser-microdissection, ventral tegmental area (VTA) and substantia nigra (SN) DA neurons were isolated from Sprague Dawley rats behaviorally phenotyped as relapse-vulnerable (n=5) or –resilient (n=6). Molecular profiling studies were performed targeting *BDNF* and other cell signaling genes.
Results: Unpaired Student's t test for each gene revealed that vulnerable rats displayed a significant decrease (~50%) in *BDNF* expression in VTA DA neurons compared to resilient controls. In contrast, *BDNF* was significantly increased (~120%) in SN neurons. A significant reduction in *AKT* (~50%) and the D2 receptor (~45%) was also observed in SN neurons of vulnerable rats.
Conclusions: Following protracted cocaine abstinence (~2 months) vulnerable animals displayed a unique DA neuron molecular profile compared to resilient controls. This pattern of *BDNF* expression may reflect the different time points at which these dopamine systems become engaged in drug-seeking. The current data supports previous findings implicating altered BDNF, AKT, and DA receptor signaling in addiction susceptibility.
Financial Support: NHMRC, HMRI

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IMPLEMENTATION OF AN ELECTRONIC INFORMATION SYSTEM TO ENHANCE PRACTICE AT AN OPIOID TREATMENT PROGRAM.

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Aims: The Addiction Research and Treatment Corporation is a medication-assisted opioid treatment program, also providing primary care (including HIV care) to approximately 2,800 predominantly minority adults in New York City. We received National Institute on Drug Abuse R01 funding to study implementation of an electronic health information system.
Methods: The domains of Quality, Risks, Productivity, Satisfaction, and Finances were evaluated utilizing a pre-post implementation study design. Subsequent to the research, we exploited system capabilities to measure Outcomes for HIV disease, diabetes mellitus, and hypertension for 100% of patients under care for these conditions.
Results: For the Quality domain, annual medical assessments and annual, 30-day, and 90-day multidiscipline assessments were timely for 83%, 70%, 72%, and 42% of cases, respectively, pre-implementation; and 97%, 96%, 87%, and 70% respectively, post-implementation. All results were highly significant. Hepatitis C viral load was appropriately performed in 85% of cases pre-implementation and 81% post-implementation; a non-significant difference. For Risks, the number of events was too low to detect a statistically meaningful change. For Satisfaction, there was no change for patients and a non-significant upward trend post-implementation for staff. Productivity declined post-implementation; reaching statistical significance for counselors. Finances did not change significantly. Outcomes for HIV disease (suppressed viral load), diabetes mellitus (HgbA1C <7), and hypertension (BP < 140/90) showed improvement over the course of a 1-year timeframe.
Conclusions: Despite only modest research results, we can now demonstrate system capabilities that improve patient outcomes, the key measure of patient status
Financial Support: Research supported by the National Institute on Drug Abuse (R01 DA022030)

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ASSOCIATION OF OBJECTIVE AND PERCEIVED NEIGHBORHOOD CHARACTERISTICS WITH TOBACCO USE AMONG YOUNG ADULTS.

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Aims: To examine the association between neighborhood disorder (ND) and tobacco use among young adults.
Methods: In this cross-sectional study participants (n=591) were sampled from the Johns Hopkins Baltimore Prevention Project's second generation prevention trial. The sample was predominately African-American (86.5%), male (52.3%), on average 19.1 years old, and 19.3% used tobacco in the past month. The Neighborhood Inventory for Environmental Typology (NIfETy) Instrument was used to assess ND objectively (e.g., abandoned buildings). The Neighborhood Environment Scale (NES) was used to assess perceptions of ND. Spearman correlations and logistic regression models were used to test the hypotheses that objective and perceived measures of ND would be correlated, as well as significantly associated with past month tobacco use.
Results: The correlation between the objective assessment of ND, and perceptions of neighborhood drug involvement was: [rho= 0.09 (p-value = 0.08)]. The correlation between the objective assessment of ND, and perception of neighborhood social cohesion was: [rho= -0.07 (p-value = 0.16)]. Objective ND (adjusted odds ratio [AOR] = 1.26; 95% confidence interval [CI]=1.03-1.55), and perceptions of neighborhood drug involvement (AOR= 1.17; 95% CI = 1.07, 1.27) were significantly associated with past month tobacco use.
Conclusions: Objective measures and perceptions of the physical environment have varying levels of influence on tobacco use among young adults. Remedying one facet of ND may not necessarily influence the others, thus comprehensive environmental interventions are warranted.
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EFFECTS OF THE SHORT-ACTING KOP-R ANTAGONIST [D-TRP]CJ-15,208 ON COCAINE SELF-ADMINISTRATION, LOCOMOTOR ACTIVITY, AND FOOD INTAKE IN MALE C57/BL6 MICE.

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Aims: Cocaine abuse remains an important public health issue. This study was designed to test how the short-acting KOP-r antagonist tetrapeptide [D-Trp]CJ-15,208 (cyclo[Phe-D-Pro-Phe-D-Trp]) affects cocaine self-administration (SA), cocaine-induced locomotor activity and food intake.
Methods: 1) Male C57/BL6 mice acquired cocaine SA (0.5 mg/kg/infusion, FR1) for 7 consecutive days. Half of the mice were injected with [D-Trp]CJ-15,208 (20 mg/kg, s.c.) and half were injected with vehicle before cocaine SA daily for 7 days. 2) To determine the effect of [D-Trp]CJ-15,208 on cocaine-induced locomotor activity, mice were injected with either compound or vehicle before cocaine injection (15 mg/kg, i.p.) and locomotor activities were recorded. 3) To assess the effect of [D-Trp]CJ-15,208 on food intake, mice were injected with compound or vehicle and the amount of food consumed over a 2-hour period was measured.
Results: 1) Mice injected with [D-Trp]CJ-15,208 had attenuated cocaine SA compared to controls. 2) Mice pre-treated with [D-Trp]CJ-15,208 did not differ in their locomotor activity either before or after cocaine injection compared to controls. 3) Mice injected with [D-Trp]CJ-15,208 before food exposure did not differ in their food intake from controls.
Conclusions: These studies show that [D-Trp]CJ-15,208 produced a decrease in daily cocaine SA in mice. This effect of [D-Trp]CJ-15,208 was neither due to a decrease in cocaine-induced locomotor activity nor accompanied by decreases in food intake. These data support future studies of short-acting compounds with KOP-r antagonist effects as potential pharmacotherapeutic approaches against cocaine addiction.
Financial Support: NIH-NIDA 1R01DA029147-01A1 (YZ), NIH-NIDA 1R01DA032928-01 (JA) and NIH-NIDA P60 DA05130 (MJK).

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THE IMPACT OF SATIVEX® ON COGNITIVE FUNCTION DURING TREATMENT FOR CANNABIS WITHDRAWAL.

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Aims: To determine the effect of a combination Δ9-THC/cannabidol medication during cannabis withdrawal on indices of cognitive performance related to driving and occupational safety.
Methods: Cannabis-dependent individuals (n=51) participated in a double-blind RCT of placebo vs. Sativex® (max. dose 21.6mg THC and 20mg cannabidol per 6 hours) during a 9 day inpatient admission for cannabis withdrawal. Cognitive assessments were taken at baseline, day 3 (peak withdrawal) and day 7 (≥15 hours after last dose). Tests assessed response speed (Reaction Time Index), adaptive inhibition (Stop Signal Task), planning (Stockings of Cambridge) and vigilance (Rapid Visual Information Processing).
Results: ANCOVA-adjusted analyses demonstrate that during peak dosing/withdrawal (day 3) Sativex-treated participants were slower (15ms, Hedge's g=-0.6) but more accurate (g=0.7) during complex reaction time. Response inhibition accuracy was improved (g=0.5) but required more time for successful inhibition (<25ms, g=-0.6). During vigilance, target response was moderately delayed (<40ms, g=-0.4) but accuracy equivalent to controls. Planning was unaffected (g<|0.2|). At day 7 (residual), no meaningful differences (g<|0.4|) were apparent in planning or vigilance, but the superior performance on response inhibition (g=0.5) and speed decrement on complex reaction time (g=-0.5) remained.
Conclusions: Sativex® produced moderate magnitude reductions in speed but similar magnitude improvements to accuracy and inhibition in comparison to unmedicated individuals during cannabis withdrawal. These speed decrements are of similar or smaller magnitude to that produced at a blood alcohol concentration of 0.05. This suggests that effects of Sativex® on cognitive performance are not a barrier to further trials in community-based services.
Financial Support: National Health and Medical Research Council

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A CONTROLLED EVALUATION OF ABSTINENCE-BASED INCENTIVES AND BEHAVIORAL PARENT TRAINING FOR ADOLESCENTS WITH CANNABIS USE DISORDERS.

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Aims: A prior study demonstrated that an intervention comprising behavior therapy (BT), clinic- and parent-delivered, abstinence-based contingency management (CM), and behavioral parent training (BPT) improved abstinence rates for teens with cannabis use disorders. The present trial was designed to replicate and extend these findings by isolating the effect of the parent-delivered treatment components and testing the multi-component intervention with a more diverse sample.
Methods: Three 14-week treatments were compared in a randomized trial: (1) BT only (motivational enhancement therapy and cognitive-behavioral therapy); (2) BT/CM; and (3) BT/CM/BPT. Participants were 153 teens (89% male) aged 12-18 and 208 parents/guardians; 55% were African American and 43% Caucasian. Primary outcomes focused on cannabis abstinence as determined by twice-weekly urine toxicology testing during treatment, and testing at 3, 6, and 12-month follow-ups.
Results: The number of cannabis-negative tests observed during treatment was greater for BT/CM than BT only (p<.05), but BT/CM/BPT and BT only did not significantly differ (p=.08). More teens achieved 4 weeks of continuous abstinence in BT/CM (65%) and BT/CM/BPT (59%) than in BT only (35%) (p< .01). At the end of treatment, more teens were abstinent in BT/CM (59%) than BT only (33%) (p<.02), but again BT/CM/BPT (49%) and BT only did not significantly differ (p=.14). Abstinence at the 3, 6, and 12-month assessments no longer showed significant differences among conditions.
Conclusions: Findings demonstrate that adding CM to BT engenders abstinence during treatment. Adding BPT did not provide additional positive effects on achievement or maintenance of abstinence. This study did not demonstrate enduring effects of CM on abstinence. Discussion will focus on the need to develop interventions strategies for nonresponders, and to continue exploration of effective maintenance interventions.
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AMPHETAMINE-TYPE STIMULANT USE AND UNPROTECTED SEX IN MEN WHO HAVE SEX WITH MEN IN VIETNAM.

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Aims: Amphetamine-type stimulant (ATS) use is associated with increased HIV risk behaviors and transmission in industrialized countries but little is known about ATS use among men who have sex with men (MSM) in Vietnam. We hypothesized that ATS use is associated with unprotected sex among MSM.
Methods: We conducted a cross-sectional survey in 2011 of 270 MSM recruited using community-based respondent-driven sampling in Hanoi (n=100), Danang (n=70) and Ho Chi Minh City (n=100). Eligible participants (age 18-45 years having sex in the past 30 days) were asked about sociodemographic characteristics, illicit drug use including ATS, and unprotected sex (not always using condoms in the past 12 months). We tested the association between current ATS use (past 90 days) and unprotected sex using multivariable logistic regression adjusting for education, living situation, heroin use, number of sexual partners, and city.
Results: Participants had a mean age of 23.3 (SD 5.7) years; 42.8% had education > high school, 14.1% of MSM were living with a spouse or sexual partner and 13.3% also used heroin. ATS use was prevalent with 85.9% reporting lifetime use and 73.3% having used in the past 90 days. No participants reported injecting ATS; 55.9% reported oral intake and 37.4% smoked ATS. First-time ATS use was in the context of peer pressure (69.6%) curiosity (57.0%), concomitant alcohol use (51.9%) with friends (84.1%) or sexual partners (13.7%). 62.0% reported having unprotected sex with a mean of 3 (SD 4.3) sexual partners. In multivariable analysis, higher education (aOR 0.32, 95% CI 0.17 0.61), and current ATS use (aOR 2.0, 95% CI 1.08 3.7) were associated with having unprotected sex.
Conclusions: Recent ATS use was prevalent in our sample of MSM in Hanoi, Danang and Hochiminh City and was associated with unprotected sex, suggesting that interventions to reduce ATS use in MSM may be indicated to reduce behaviors associated with HIV transmission in Hanoi.
Financial Support: VH-ATTC – TI23603; UNODC VNM/J93; Fulbright Scholar to Vietnam 2012-2013

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FEDERAL PARITY DOES NOT LEAD TO LARGE INCREASES IN SPENDING ON SUBSTANCE USE DISORDER TREATMENT: RESULTS FROM YEAR 1.

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Aims: In 2008, Congress passed legislation requiring health insurers to equalize private insurance coverage for mental health and substance use disorder services with coverage for general medical services (parity). We sought to examine the effects of federal parity on substance use disorder treatment in the first year after passage.
Methods: We used a difference-in-differences design to compare changes in outcomes among health plan enrollees in the years before and after implementation of federal parity (2009-2010) with changes in outcomes among a comparison group of enrollees previously covered by state substance use disorder parity laws. We used claims data from 298,339 Aetna Inc. health plan enrollees in fully insured and self-insured plans in ten states with substance use disorder state parity laws. We examined the proportion of enrollees using any substance use disorder treatment; annual total spending on substance use disorder treatment; out-of-pocket spending on substance use disorder treatment and three substance use disorder performance measures: identification, treatment initiation and treatment engagement.
Results: We found that federal parity led to no change in the proportion of enrollees with any substance use disorder treatment and no change in out-of-pocket spending on substance use disorder treatment per user. There was a small increase in total spending on substance use disorder treatment per enrollee ($9.88, 95% CI: 1.74, 17.78). Federal parity led to a small increase in identification (0.08 percentage points, 95% CI: 0.003, 0.15), but no change in either treatment initiation or treatment engagement.
Conclusions: We conclude that the inclusion of substance use disorder services in the federal parity law did not result in substantial increases in health plan spending. It will be critical to study whether first year results persisted after requirements clarifying the application of non-quantitative treatment limits took effect in 2011.
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CLIENT REASONS FOR POOR ENGAGEMENT EARLY IN SUBSTANCE ABUSE TREATMENT.

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Aims: Numerous prediction studies have identified variables (e.g., substance use and psychiatric severity) associated with attrition from outpatient substance abuse treatment (SAT). Very few studies have examined factors associated with dropout from the client's perspective. Those that have indicate that dissatisfaction with aspects of treatment as well as individual status factors are reported reasons for dropout. The present study rates clients' self-reported reasons for early attrition from outpatient SAT.
Methods: Clients (N=106) recently admitted to two outpatient SAT programs, who irregularly attended treatment during the first 2-3 weeks, were contacted for a brief telephone motivational intervention. During this call they were queried about reasons for lack of attendance, which were then abstracted and coded.
Results: Clients reported various and multiple reasons for poor early engagement in treatment that roughly paralleled those reported for dropping out of treatment by clients in previous studies. These reasons can be categorized as: Client Factors—particularly medical and psychological problems, and acute life stressors; Treatment Factors including issues with clients and staff, as well as the schedule and nature of the treatment itself; and Environmental or Logistical Factors such as transportation, finances, and competing employment demands.
Conclusions: Client attributions for outpatient treatment attrition are not fully parallel with variables identified in prediction studies obtained via patient assessments. Further, clients identify many issues that appear to be actionable in some way, and that if prepared for or dealt with by the clinics at both the programmatic and individual client levels, could improve retention.
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CURRENT THINKING ON THE PREMARKETING EVALUATION OF ABUSE-DETERRENT OPIOID FORMULATIONS.

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Aims: To provide an overview of the Food and Drug Administration (FDA) current thinking about the studies that should be conducted to demonstrate that a formulation has abuse deterrent (AD) properties.
Methods: Abuse and misuse of prescription opioid analgesics is a serious and growing public health problem. Consequently, the development of AD formulations that are less prone to abuse or misuse is a public health priority. To that end, the Center for Drug Evaluation and Research at FDA is developing a guidance regarding the evaluation of AD opioid formulations.
Results: A phased three tier approach for premarketing assessment has been proposed for formulations with potential AD features. The first tier consists of in-vitro manipulation and extraction studies, aimed to evaluate the ease with which AD features of a new formulation can be defeated or partially compromised under experimental conditions. Pharmacokinetic/pharmacodynamic studies constitute the second tier. These studies are designed to understand the in-vivo properties of the new formulation by comparing the pharmacokinetic profiles of the "manipulated" formulation with the intact formulation and other comparator drugs through one or more routes of administration, and to collect pharmacodynamic outcomes such as adverse events associated with the administration of the manipulated formulation. The third tier consists on evaluating the relative abuse potential of the AD formulation to that of a positive control and placebo in human abuse potential studies.
Conclusions: The development of formulations with abuse-deterrent properties represents an evolving area of research. Abuse-deterrent technologies and the methodology for evaluating those technologies are rapidly evolving. Therefore, in addition to retaining a flexible, adaptive approach to the evaluation of AD formulations, there is considerable potential for additional scientific work to aid in the efforts to develop and assess AD formulations.
Financial Support: N/A

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METHYLPHENIDATE SELF-ADMINISTRATION INCREASES THE POTENCY AND REINFORCING EFFECTS OF RELEASERS THROUGH A DOPAMINE TRANSPORTER MECHANISM.

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Aims: Intravenous abuse of methylphenidate (MPH) has become prevalent, which is alarming given the lack of research on its consequences. We examined the effects of MPH self-administration (SA) on the nucleus accumbens core (NAcc) dopamine (DA) system, as changes can influence reward and reinforcement. The DA transporter (DAT) is the primary site of action of psychostimulants, thus we assessed the potency of compounds to inhibit the DAT following MPH SA. Further, we assessed the reinforcing efficacy of cocaine (COC), MPH, and amphetamine (AMPH). MPH SA resulted in increased DAT levels, thus we increased DAT levels by transgenic over-expression [DAT(tg)] to determine if it was sufficient to cause the MPH SA-induced effects.
Methods: Rats underwent fixed ratio one (FR1) SA. Kinetics of stimulated DA signals were measured with *in vitro* voltammetry. COC, MPH and AMPH were applied to slices to assess potency. To assess reinforcing efficacy animals were switched to a threshold procedure (Oleson et al., 2012) for AMPH, COC, and MPH. For locomotor analysis mice were placed into locomotor chambers, injected with drug and monitored.
Results: MPH SA increased uptake rates and DAT levels. MPH SA increased the potency and reinforcing efficacy of AMPH and MPH, with no effect on COC. We replicated the effects with DAT(tg) mice, demonstrating increased AMPH and MPH, but not cocaine, -induced potency and locomotor activity, suggesting that increased DAT levels are the mechanism by which theses effects occur.
Conclusions: MPH SA resulted in enhanced potency and reinforcing efficacy of AMPH and MPH but not COC. These effects are likely through DAT increases as increasing DAT levels [DAT(tg)] had the same effects. This has implications for MPH abusers as well as individuals with differential DAT levels at baseline (eg. ADHD, drug abusers) as it suggests an enhanced susceptibility to the reinforcing properties of some psychostimulants.
Financial Support: R01DA024095, R01DA03016, T32DA007246, F31DA031533

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USE OF THE BEING SAFE IN TREATMENT (BEST) FEEDBACK TOOL TO INCREASE COUNSELOR KNOWLEDGE OF PATIENT SEXUAL BEHAVIOR.

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Aims: Determine if providing the Being Safe in Treatment (BEST) feedback report to substance abuse treatment counselors increased counselors' knowledge about their patients' sexual risk behavior.
Methods: The BEST was administered to 48 men and 31 women in outpatient treatment. Participants were randomly assigned to receive (RR) or not receive (NR) a BEST feedback report in a 2:1 ratio. Those receiving a feedback report had the option of providing a copy of the report to their counselor (CR). The BEST assessment was repeated 3 months later and the patient's counselor was asked in a self-report survey if the patient in the prior 90 days was: 1) sexually active; 2) had multiple sexual partners; 3) engaged in sex under the influence of drugs or alcohol, and 4) engaged in unprotected sex. Each variable was coded a 1 when there was concurrence between the counselor's response and the actual behavior reported by the patient. These four variables were summed to obtain an overall congruence measure with a range from 0-4; higher scores indicating greater congruence between counselor's belief about the patient's sexual behavior and patient's actual self-reported behavior.
Results: Congruence between counselor belief and actual patient self-reported behavior was highest for having multiple partners (79.8%) and being sexually active (73.4%), whereas congruence was lower for sex under the influence (65.4%) and engaging in unprotected sex (59.5%). The summed congruence value for CR patients (n=29) was significantly higher (M=3.17, sd=0.85) than NR patients (n=25, M=2.40, sd=1.16) and RR patients (n=25, M=2.72, sd=0.9, F=4.13, p=0.02).
Conclusions: A counselor receiving a BEST feedback report was associated with the counselor having increased knowledge about the patient's sexual behavior. Future studies are needed to determine if increased counselor knowledge can contribute to reduced patient sexual risk.
Financial Support: NIDA grants R21DA022940 (D. Calsyn, PI), U10 DA13714 (D. Donovan, PI), K23 DA025678 (Bryan Hartzler, PI).

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A QUALITATIVE STUDY OF YOUNG ADULTS' PERCEPTIONS OF MODIFIED-RISK TOBACCO PRODUCTS FOR SMOKING CESSATION.

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Aims: Through the Family Smoking Prevention and Tobacco Control Act, the Food and Drug Administration has the potential to regulate modified risk tobacco products (MRTPs), or tobacco products that are sold or distributed for use to reduce harm or the risk of tobacco-related disease. The objective of this study is to examine young adults' perceptions of MRTPs (electronic cigarettes and dissolvables) for cigarette smoking cessation.
Methods: Eight focus groups will be conducted with a sample of 18-25 year old smokers and non-smokers attending two public colleges in Connecticut; 4 focus groups (N=29 young adults) have been completed and four will be completed in early 2013. Groups were stratified by gender and smoking status. A standard focus group guide was used to ask participants about their knowledge of MRTPs (electronic cigarettes and dissolvables) and usefulness in smoking cessation. Group discussions were recorded, transcribed, and examined using thematic analysis.
Results: Evidence collected to date indicates that smokers and non-smokers were aware of electronic cigarettes, but not dissolvables. Smokers believed that electronic cigarettes were more appealing than existing smoking cessation aids because they mimicked the act of smoking, could be flavored, and did not have widely known side effects. Many smokers experimented with electronic cigarettes and reported that they were not as satisfying as traditional cigarettes. Smokers would exclusively switch to electronic cigarettes when attempting to quit. Smokers and non-smokers did not believe dissolvables were appealing for smoking cessation because they did not mimic smoking, and did not appear tasty or pleasurable.
Conclusions: Both smokers and non-smokers have high awareness of electronic cigarettes but not dissolvables. Evidence from the remaining four focus groups will also be presented. This formative qualitative data suggests that electronic cigarettes appeal to young adults as smoking cessation aids.
Financial Support: This work was supported by the National Institute on Drug Abuse grant P50DA009241.

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SMOKING PREVALENCE AND EXPOSURE TO SECOND HAND-SMOKE IN MEXICAN PREGNANT WOMEN.

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Aims: The prevalence of smoking among women in Mexico has increased to 12.6 % of the adult population. The aims were to assess the prevalence of tobacco smoking and of exposure to second hand smoke (SHS) among pregnant women in a major pre-natal care clinic in Guadalajara.
Methods: Face-to-face interviews were conducted with 454 women attending the pre-natal care clinic to assess smoking and exposure to SHS. Patients found to be smokers received brief intervention and were referred to a smoking cessation program for pregnant women.
Results: The patients' mean age was 24.4 (± 7.5) years; their mean months of pregnancy was 6.7 (± 1.9). Regarding smoking, 3.0 % were active smokers, while 27.5% had smoked before pregnancy. Regarding SHS, 49.5 % lived on average with 1.4 (± 1) smokers who smoked a mean 3.9 cigarettes in their presence. In particular, this included a husband/partner (31.0%), father (17.3%), mother (12.5 %), parents in-law (6.9%), brothers (9.1%), sisters (4.0%), brothers in-law (2.5%), uncles/aunts (1.6%), and other relatives (2.5%). Outside their homes (including work), 22.5% of the women were exposed to a mean of 3.5 (± 3.3) persons who consumed a daily mean of 7.9 (± 9) cigarettes.
Conclusions: The prevalence of women smoking during pregnancy was relatively low in this sample. Most of the women reporting lifetime histories of smoking had stopped smoking by the time they were pregnant. The prevalence, however, of exposure to SHS in the sample (49.5%) was higher than in the Mexican general population (39.2%)—a disconcerting situation. The findings from this sample need to be replicated at other sites. To our knowledge this studythe is the first of its kind in Mexico, underscores the need to find and implement ways to help pregnant patients limit their exposure to SHS.
Financial Support: This project is funded by the Programa de Mejoramiento de Profesorado (PROMEP) of the Mexican Education Department (SEP).

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PARADOXICAL NORMALIZATION OF RISK-TAKING BY MODAFINIL IN CHRONIC COCAINE USERS.

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Aims: Modafinil, a wake-promoting agent used to treat sleep disorders, is thought to enhance cognition. Although modafinil has shown promise as an agonist-based pharmacotherapy for the treatment of cocaine dependence, it is unknown to what extent cognitive effects may play a role in such treatment. We examined the effect of modafinil on the Balloon Analogue Risk Task (BART), a behavioral measure in which higher scores are purported to reflect a greater propensity for risk-taking.
Methods: Twenty-six cocaine dependent individuals enrolled in a randomized clinical trial of modafinil 400mg (n=11) versus placebo (n=15) were administered the BART on 3 occasions during the eight week (2 weeks inpatient/6 weeks outpatient) treatment protocol.
Results: BART scores among placebo treated participants were markedly lower than previously reported in healthy participants and lower than observed in a healthy cohort in our laboratory, suggesting a propensity for less 'risk-taking'. However, modafinil treatment was associated with significantly higher BART scores ($p<0.05$), which were comparable to scores in healthy persons. BART scores increased across the three administrations, with no time by treatment group interaction.
Conclusions: As propensity toward risk taking is typically associated with higher BART scores as well as increased risk for substance use, our findings may reflect a novel aspect of cognitive impairment related to chronic cocaine use. Notably, the low BART scores reflect highly suboptimal performance on the task, and the observed effect of modafinil may indicate a normalization of this impairment and have implications for treatment outcome.
Financial Support: This work was supported by a grant from the National Institute on Drug Abuse (R01 DA011744) and by the State of Connecticut Department of Mental Health and Addiction Services.

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WHAT'S LONELINESS GOT TO DO WITH IT? OLDER WOMEN'S USE OF BENZODIAZEPINES.

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Aims: This research sought to explore the experience of benzodiazepine (BZD) use in a sample of older, BZD-using, community-dwelling women.
Methods: Following a phenomenological design, women age 65 and older who reported regular use of a BZD over the previous 3 months were recruited to complete three semi-structured interviews on their experiences of BZD use. Interviews were digitally recorded and subsequently transcribed. Data were coded and analyzed for experience in order to access what was significant to informants. Coding was an iterative process of defining what the data was concerned with and codes were organized into themes and served as the units of analysis.
Results: A significant theme that emerged from the data was informants' reports of being or feeling "alone" and the influence this had on their BZD use. Informants were not directly asked about loneliness or feeling alone, but this theme was brought up by seven informants, all of whom lived alone (four who were widowed, two who were divorced, and one who never married) and reported feeling alone or lonely. Informants suggested that loneliness created feelings of depression or sadness and that BZDs were helpful in coping with these negative moods. In comparison, a few informants reported that the stress of providing care for or living in close proximity to family members outweighed the stress of potentially being alone.
Conclusions: These findings support previous research that has found living alone or feeling lonely to be risk factors for the use of BZDs among older women. Treating isolation, which is a social problem, with medications, wrongly turns this social experience into an individual issue. Replacing social supports, social activities, and human companions who offer help or security with prescription medications perpetuates inappropriate and ageist treatments for older adults.
Financial Support: This research was supported by NIDA through a NRSA award (F31DA025391) and through the Drug Dependence Epidemiology Training Program (T32DA007292), with the Johns Hopkins University Bloomberg School of Public Health.

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HYPOACTIVE BOLD RESPONSE TO GENERAL EMOTIONAL STIMULI AMONG COCAINE-DEPENDENT WOMEN.

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Aims: Many brain regions activated by emotionally salient stimuli overlap with limbic regions involved with drug-taking behavior. In addition, gender affects both general emotional response and mood-induced drug use, with women typically having a stronger response to negative stimuli than men. The purpose of the current study was to determine 1) whether cocaine users had a different response to emotionally salient pictures than controls and 2) whether this was particularly apparent in females.
Methods: In this functional MRI experiment, 14 cocaine-dependent (6m, 8f) and 15 non-drug using individuals (7m,8f) viewed blocks of positive, negative and neutral images selected from the International Affective Picture System. The data were modeled using standard voxel-based methods. The BOLD response to positive and negative images (relative to neutral) was compared between groups with respect to gender.
Results: Cocaine users had less activation in mesolimbic regions than controls in response to positive and negative images. Among the men, there were no significant differences between cocaine users and controls when viewing positive pictures. When viewing negative pictures, cocaine-dependent men had significantly less activity in the posterior cingulate than control men. Among the females however, both positive and negative images evoked a significantly lower BOLD response in the medial prefrontal cortex from the cocaine users relative to the controls.
Conclusions: These results demonstrate that while cocaine using males differ from controls only in response to negative images, the female cocaine users have a blunted response in the frontal cortex to emotional stimuli independent of valence. This may be associated with a stronger relationship between mood and drug use behavior in female than males. While many studies in the substance dependence literature involve primarily men, these data highlight the need to consider gender in future behavioral and cognitive treatment approaches among cocaine users.
Financial Support: K01DA027756, 5T32DA007288

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COMPARISON OF SENTENCED INMATES' DRUG USE PATTERNS BEFORE AND DURING INCARCERATION.

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Aims: Drug users are over represented in correctional settings and drug use in prison is a worldwide phenomenon, yet little is known about patterns in drug use as individuals transition from community to prison and their implications for services planning. We report results of a study that compared drug use patterns prior and during imprisonment in a representative sample of the sentenced inmate population in the Puerto Rico prison system.
Methods: 1,179 inmates (89.7% response rate) participated in a structured questionnaire administered through 2 interview modalities: Computer Assisted Personal Interview for social and health variables; Audio Computer Assisted Self Interview for sensitive information. A latent transition analysis was conducted with MPLUS using as class indicators variables representing 6 types of illegal drug use before and during the current incarceration. The model assumed measurement invariance of the classes obtained before and during incarceration.
Results: A 3 class solution was chosen based on good model classification accuracy (entropy .85). Before incarceration: Class 1: inmates with low probability of using any drug (23%), Class 2: inmates with a pattern of using all drugs with a moderate-high probability (31%), Class 3: inmates with a high use of marihuana and low-moderate use of cocaine and non-prescribed medications (45%). Drug use patterns during imprisonment: 55% of those in the high drug use class before incarceration remained in the same class. 33% transitioned to the low drug use class and 14% to the class that mainly uses marihuana. 1% of those in the class with low probability of drug use transitioned to the class of heavy drug use. 7% of those who mainly used marihuana and non-prescribed medications transitioned to the heavy drug use class.
Conclusions: These findings should inform prevention interventions. Half of the inmates persist in their drug use once in prison and 8% transitioned from soft to hard drugs with serious public health implications given the frequency of injection drug use in this context.
Financial Support: NIDA Grant # 2R24DA024868-03

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THE ROLE OF SEROTONIN 2A AND 2C RECEPTORS IN TRYPTAMINE HALLUCINOGENS N,N-DIMETHYLTRYPTAMINE AND N,N-DIISOPROPYLTRYPTAMINE.

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Aims: Hallucinogens have been used for centuries yet compared to other drug classes, relatively little is known about their mechanism of action. Classic hallucinogens are grouped into tryptamine, phenethylamine and ergot alkaloid classes of hallucinogens. Serotonin (5-HT) 2A and 2C receptors are primary targets for classic serotonin-mediated hallucinogens and presumed to be targets for the two tryptamine hallucinogens N,N-dimethyltryptamine (DMT; visual hallucinations) and N,N-diisopropyltryptamine (DiPT; auditory distortions). The roles of these receptors in attenuating the effects DMT and DiPT were assessed.
Methods: Drug discrimination, head twitch and radioligand binding assays were used. Rats were trained to discriminate DMT or DiPT from saline. Antagonists selective for 5-HT2AR (MDL100907) and 5-HT2CR (SB242084) were used to attenuate the discriminative stimulus effects. MDL100907 was used to attenuate drug-induced head twitches in mice. Radioligand binding was performed at the 5-HT2CR in HEK cells for DiPT and compared to pre-existing data for DMT.
Results: MDL100907 fully blocked the discriminative stimulus effects of DMT, but only partially blocked DiPT. SB242084 partially attenuated the discriminative stimulus effects of DiPT, but minimally attenuated DMT's effects. Both compounds produced head twitches (DiPT>DMT), which were blocked by MDL1000907. DiPT and DMT had similar binding and were fully efficacious at the 5-HT2C receptor, but DiPT was ~ 20 times less potent at stimulating IP-1 formation.
Conclusions: 5-HT2AR and 5-HT2CR play different roles in mediating the discriminative stimulus effects of DMT and DiPT. 5-HT2AR is essential for both compounds, whereas 5-HT2CR may be more important for the stimulus effects of DiPT. DMT has a pharmacological profile similar to other classical hallucinogens. No drug tested was able to completely block DiPT-like effects, suggesting other or multiple receptors may be important.
Financial Support: NBA T32 AG020494 and NIH N01DA-7-8872

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LATENT CLASS ANALYSIS OF NON-OPIOID DEPENDENT ILLEGAL PHARMACEUTICAL OPIOID USERS IN OHIO.

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Aims: The illegal use of pharmaceutical opioids has resulted in increases in opioid dependence and unintentional overdose deaths. This study uses latent class analysis to characterize drug use practices among a community-based sample of 18-23 year-olds actively engaged in illicit pharmaceutical opioid use, yet not opioid dependent.
Methods: Respondent-driven sampling was used to recruit 396 participants. Latent class analysis was used to identify sub-groups of drug users based on drug types and frequency of use. Multinomial logistic regression was then used to estimate the significance of covariates in predicting class membership.
Results: The mean age was 21.0, 54.5% were men, and about 44% were African American. The mean age of opioid initiation was 16.9 years. About 32% used opioids to "get high" only, 15.9% to "self-medicate," and 52.3% used them to "get high" and "self-medicate." A two-class model was chosen. Individuals in Class 1 used non-prescribed opioids less frequently than individuals in Class 2. Conversely, individuals in Class 1 used all other drugs more frequently, compared to individuals in Class 2. Being non-white, using pharmaceutical opioids to self-medicate, and having less educational achievement were significantly associated with membership in Class 2 ("pharmaceutical opioid-focused users"). A greater proportion of individuals in Class 1 ("polydrug users") met DSM-IV criteria for lifetime alcohol, marijuana, amphetamine, and tranquilizer use disorders.
Conclusions: Differences in drug use practices between the two groups, coupled with differing rationales for pharmaceutical opioid use, suggest the need for tailored interventions.
Financial Support: NIDA grant R01DA23577 (R.G. Carlson, PI).

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POSITIVE AFFECT IS A SOURCE OF RESILIENCE AMONG TREATMENT-SEEKING METHAMPHETAMINE USERS.

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Aims: Revised Stress and Coping Theory proposes that positive affect serves adaptive functions, but scant research has examined whether or how positive affect is associated with decreased substance use. We hypothesized that cognitive-behavioral change processes would mediate the association between greater positive affect and decreased stimulant (i.e., cocaine, crack, and methamphetamine) use.
Methods: A total of 86 methamphetamine-using men who have sex with men (MSM) completed the baseline assessment for substance abuse treatment outcome study which included measures of positive and negative affect, cognitive-behavioral change processes, self-reported substance use in the past 30 days, and a urine sample for toxicology screening.
Results: Most participants were HIV-positive (67%), Caucasian (66%), and middle-aged (M = 43, SD = 9). Positive affect was not directly associated with decreased stimulant use ($p > .05$). After controlling for demographic characteristics and negative affect, positive affect was independently associated with greater positive reappraisal coping (Beta = .67, $p < .01$), problem solving coping (Beta = .62, $p < .01$), and self-efficacy for managing methamphetamine triggers (Beta = .27, $p < .05$). Positive affect was also independently associated with higher scores on a measure of the action stage of change (Beta = .39, $p < .01$) and increased abstinence-specific social support (Beta = .60, $p < .01$). Positive affect was indirectly associated with significantly lower odds of reporting binge (2 or more days in a row) stimulant use (OR indirect = 0.11; 95% CI = 0.03 – 0.45) and decreased odds of providing a urine sample that was reactive for stimulants (OR indirect = 0.21; 95% CI = 0.05 – 0.89) via these cognitive-behavioral change processes.
Conclusions: Positive affect may assist individuals with avoiding stimulant use by reinvigorating cognitive-behavioral change processes.
Financial Support: This research was funded by the California HIV/AIDS Research Program.

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ABUSE OF PRESCRIPTION OPIOIDS AND ILLEGAL DRUGS AFTER INTRODUCTION OF ABUSE-DETERRENT OPIOID FORMULATIONS IN THE NAVIPPRO® SURVEILLANCE NETWORK.

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Aims: Increased morbidity and mortality related to abuse of prescription (Rx) opioids shifted pharmaceutical industry focus to drug formulations with technologies aimed to deter abuse via tampering and alternative routes of administration. To evaluate the impact of introduction of abuse deterrent formulations (ADFs) on abuse of prescription opioids and other drugs, we examined abuse rates before and after introduction of new formulations of OxyContin® and Opana® ER for Rx opioids in general, immediate-release (IR) and extended-release (ER) opioids, as well as other drugs including sedatives/benzodiazepines, cocaine, amphetamines, marijuana, and heroin.
Methods: Quarterly prevalence of abuse of the target drugs was estimated among individuals assessed for substance abuse problems from January 1, 2008 to September 30, 2012 using the NAVIPPRO® Addiction Severity Index-Multimedia Version (ASI-MV®). The ASI-MV is a computer-administered, clinical interview that collects self-report data from adults on past 30-day drug abuse, including Rx opioids. ASI-MV respondents differentiate abuse of prescription products using screen images.
Results: In the sample of 225,829 assessments (X = 11,886 per quarter) abuse of any Rx opioid increased (17% - 22% of assessments), as did abuse of total ER opioids (10% - 13%) and total IR opioids (13% - 15%). ER morphine and hydrocodone abuse did not change. Buprenorphine abuse increased (2% - 7%) as did ER oxymorphone (0.2% to a high of 1.5% just prior to release of the reformulated Opana ER; afterwards averaged 1.1% for the next three quarters). Of the other drugs examined, abuse of sedative/benzodiazepine and cocaine did not change. Marijuana abuse increased steadily over the time period (21% - 28%). Amphetamine and heroin abuse rates remained steady until the quarters following release of reformulated Opana ER.
Conclusions: These early findings suggest that as different ADFs enter the market, the pattern of abuse of other drugs is likely to shift. Continued monitoring is warranted.
Financial Support: Inflexxion, Inc.

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DSM-V ALCOHOL USE DISORDER SYMPTOM PROFILE IN A REPRESENTATIVE SAMPLE OF THE LARGEST METROPOLITAN AREA IN SOUTH AMERICA.

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Aims: Given the development of a new diagnostic classification (DSM-V) for alcohol use disorders (AUD), we aimed to identify cathegorical fenotipes among past year alcohol users who had at least 1 drink per month in the 12 months prior to the interview. Data came from São Paulo Megacity Project collected between 2005-2007, which is part of World Mental Health Surveys.
Methods: Latent class analysis of the 11 DSM-V symptoms was performed using Mplus software taking into account complex survey design features. Then, via weighted logistic regression models, we examined socio-demographic correlates of the DSM-V AUD latent classes, frequency of alcohol past-year use within classes, the proportion of individuals in each class endorsing DSM-IV AUD and the DSM-V severity sub-diagnosis.
Results: The best latent class model was a four-classes model. We found a "non-symptomatic class" (68.6%), a "larger amounts class" (19.6%), a "lost-control class" (8.1%)- defined by high probabilities of "use in larger amounts" and unable to cut down criteria - and a "high-symptomatic class" (3.7%). Those in the "high symptomatic class" were above 5 times more likely to be males and less likely to have a high-average income than those in the non-symptomatic class. Being in the "larger amounts" and "lost control" classes was associated with lower levels of education compared to the non-symptomatic class. Among the"high-symptomatic class", 17.3% were not classified as alcohol dependents by the DSM-IV. Among the "larger amounts class", only 5.5% had DSM-IV alcohol dependence.
Conclusions: Most alcohol users diagnosed with AUD are in the "larger amounts" class, which associated with lower levels of education. Gender and income play a role in the most problematic class. Prevention and specific treatment protocol can be designed based on this data.
Financial Support: The São Paulo Megacity Mental Health Survey is supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

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A CROSS-LAGGED ANALYSIS OF FIVE INTRAPERSONAL DETERMINANTS OF SMOKING ABSTINENCE.

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Aims: The current study examined the prospective cross-lagged relationships among five intrapersonal determinants of relapse (motivation to abstain from smoking, self-efficacy to abstain from smoking, positive affect, negative affect, and craving) and their associations with smoking abstinence during a quit attempt.
Methods: Data from 434 individuals enrolled in a longitudinal study on the social determinants of smoking cessation were used. Participants received six weeks of nicotine patch therapy, six brief counseling sessions, and self-help materials. The current study utilized data on the five intrapersonal variables collected at baseline (pre-quit) and the quit day, and abstinence status assessed one week post-quit. A model was constructed consisting of all autoregressive and cross-lagged paths from the pre-quit measures to quit-day measures, and direct paths from the quit-day measures to 1 week post-quit abstinence. Using path analysis, the model was tested for fit and then trimmed to develop the best fitting, most parsimonious model.
Results: The full model demonstrated good fit. Model trimming resulted in a final model in which only motivation and self-efficacy showed true cross-lagged relations. Further, only quit-day motivation and positive affect were direct predictors of abstinence. Pre-quit motivation and negative affect indirectly predicted abstinence through their effects on quit-day positive affect. The final model demonstrated invariance across race/ethnicity.
Conclusions: The current study sheds new light on reciprocal relationships among several key determinants of smoking abstinence, reaffirms the importance of motivation in smoking cessation, and presents novel data regarding positive affect that may have important implications for treatment development research.
Financial Support: This research was supported by NIH grants R01 DA014818, K01 CA157689, U54 CA153505, R25T CA57730-S2, and P30 CA016672, and American Cancer Society grant MRSGT-12-114-01-CPPB.

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LONGER ABSTINENCE FROM METHAMPHETAMINE IS ASSOCIATED WITH BETTER NEUROCOGNITIVE PERFORMANCE IN YOUNGER BUT NOT OLDER ADULTS.

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Aims: Although methamphetamine (MA)-related neurotoxicity may be partially reversible with sustained abstinence, whether the trajectory of neural recovery is moderated by age is not known. Given evidence of reduced neural plasticity with increasing age, we hypothesized that younger age would be associated with greater neurocognitive recovery with longer MA abstinence.
Methods: 220 individuals who met DSM-IV criteria for MA use disorders within the past 18 months were classified as either younger (mean=33.0, SD=5.3) or older (mean=46.0, SD=4.2) based on a median split. Participants underwent neuropsychological (NP), medical, psychiatric, and substance use assessments. NP outcomes included mean scaled scores (uncorrected for age) in 7 cognitive domains: speed of information processing, executive functions, verbal fluency, learning, memory, working memory, and fine-motor performance. Age groups did not differ in terms of other demographic factors, psychiatric and substance use comorbidities, total quantity of MA use, and prevalence of HIV infection (ps>.10). The older group had a significantly higher prevalence of hepatitis C infection and was older at first reported MA use (ps<.05).
Results: Multiple regressions including age group, days of abstinence from MA, and their interaction, along with HCV serostatus and age of first use of MA, significantly predicted NP performance in all cognitive domains (all ps<.05) except fine motor skills (p>.10). For speed of information processing and executive functions, there was an interaction between age and MA abstinence, whereby younger (betas = .21-.25, ps<.05) but not older (ps>.10) individuals demonstrated better performance with longer abstinence.
Conclusions: Older adults demonstrated reduced neurocognitive benefit of prolonged abstinence from MA, perhaps as a function of diminished potential for neural plasticity (e.g., synaptic remodeling) following MA-associated neurotoxicity.
Financial Support: NIH grants P01-DA12065, P50-DA026306, 5T32DA007315-09, P30-MH62512; PST4TP1 (TMARC).

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DEVELOPMENT OF AN ADOLESCENT MARIJUANA EDUCATIONAL PRESENTATION: PRELIMINARY FINDINGS.

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Aims: Marijuana use among adolescents continues to be a significant problem, with numbers suggesting over three million using marijuana in the last month and many progressing to regular use. Given the prevalence of adolescent marijuana use and the associated health risks, it is important to educate young people about marijuana's effects to redirect their perceptions prior to the onset of regular marijuana use. The objective of this study is to present a brief marijuana education session to local high school students in a non-biased fashion to determine if participants changed intentions to use and perceptions of harm.
Methods: 694 students in three local high schools received a 30 minute presentation during health classes on marijuana prevalence, and the physical, emotional, and cognitive health effects. Content and delivery was non-biased and interactive utilizing motivational techniques to offer facts and data about marijuana to empower students to make educated decisions about marijuana. Participants were given a brief voluntary and anonymous questionnaire prior to and immediately following the presentation to assess intentions to use marijuana (yes/no) and perceived harmfulness (6 items rated 0-4 for a total of 24).
Results: Descriptive analyses indicated that 18% of 694 adolescents reported smoking marijuana and 16% reported intending to use in the next 6 months. Of the current users, 13% plan to continue using and 3.7% plan to stop using in the next 6 months. Following the presentation, 1% of nonusers intend to use marijuana, 9.9% of current users plan to continue using, and 6% plan to stop using in the next 6 months. Perception of harm was significantly higher at pre-test for non-users of marijuana (M = 23.7, SD = 4.0) compared to users (M = 17.2, SD = 4.7), p<.01; however, both groups significantly increased perception of harm from pre- to post-, (p<.001).
Conclusions: High school adolescents were receptive to discussing the effects of marijuana and modified their perceptions about marijuana's harmfulness and plans to continue using following an impartial motivational presentation.
Financial Support: Supported by NIDA grant P50DA009241

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HIGH-RISK METHODS AND PARAPHERNALIA PRACTICES OF CRACK SMOKING IN MEXICO CITY.

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Aims: The smoking of crack is a recent emerging phenomenon in Mexico. To date, limited information is available on how the practice of smoking crack has emerged and spread among the local drug using subpopulations. Using analytical constructs from the Diffusion of Innovation Theory, this presentation provides an understanding of the complex processes associated with the emergence, initiation an adoption of crack use. Specifically, we document the unique high risk practices of use including preparation and paraphernalia utilized by this subpopulation of crack users.
Methods: In-depth semi-structured ethnographic interviews and observations were conducted with 150 male and female adult current crack users from neighborhoods (colonias) in three delegaciónes (boroughs) in México DF : Iztapalapa, Coyoacán and Cuauhtémoc.
Results: Qualitative results reveal a wide array of paraphernalia ranging largely from makeshift items (i.e. soda cans, glass droppers, TV or car antennas, etc.) to neighborhood store bought pipes. Common patterns of paraphernalia sharing were observed, in particular among those subjects reporting daily use of crack. Subjects describe a deep-seated subculture that is sustained by easily accessible street level crack market and an extensive network that fosters the adoption of unsafe paraphernalia practices of crack smoking.
Conclusions: Findings point to potential social and health risks that have not been addressed in the existing international literature. Our data will contribute significantly to the development of theory based HIV and STI interventions for crack using high risk populations in Mexico. More specifically, these data will contribute to designing peer-based brief interventions that address social and contextual factors associated with the innovation and diffusion of crack use in México DF.
Financial Support: This research is supported by a NIDA funded International Collaboration grant 7R21DA031376.

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THE IMPACT OF HIV ON BEHAVIORAL HEALTH SERVICES UTILIZATION AMONG PEOPLE WITH SUBSTANCE USE DISORDER OR PSYCHIATRIC DISORDER: A PROPENSITY SCORE MATCHING ANALYSIS OF MULTI-YEAR NATIONAL SURVEYS.

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Aims: A serious medical illness co-occurring with behavioral disorders complicates health care access and utilization. This study aims to estimate the impact of HIV status on behavioral health service use, depending on types of comorbid behavioral disorders.
Methods: Three years of data from the National Survey on Drug Use and Health (2008-2010) were combined for analysis. Respondents age 18 years or older with substance use disorder (SUD) or mental health disorder (MHD) were selected. One-to-one propensity score matching was performed to create three quasi-experimental "case" and "control" groups: 1) people with HIV with co-occurring SUD or MHD, vs. without HIV (n=182); 2) those with HIV and SUD vs. those with SUD only (n=102); 3) those with HIV and MHD vs. those with MHD only (n=138). Matching variables included demographics, enabling and need factors. The effect of HIV on utilization is assessed through logistic regression.
Results: Statistically significant differences of utilization (two-tailed $p<.05$) were observed between case and control groups for all three groups. The odds of utilization were 2.16 times higher in the "with HIV with SUD or MHD" group; 3.29 times higher in the "with HIV and SUD" group; 2.43 times higher in the "with HIV and MHD" group.
Conclusions: Those who also lived with HIV with comorbid behavioral health disorders are more likely to use behavioral health services. HIV increases the odds of treatment. The pattern of results suggests that state and federal initiatives to improve behavioral health access for persons with HIV have been effective.
Financial Support: None

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INFLUENCES OF HARM REDUCTION PROGRAMS ON HIV KNOWLEDGE AND RISKY BEHAVIORS AMONG INJECTION DRUG USERS IN PRISONS IN TAIWAN.

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Aims: The aims of this study are: 1) to assess HIV knowledge and risky behaviors among injection drug users (IDUs) in prisons; 2) to examine gender differences in HIV knowledge and risky behaviors among this population; and 3) to examine whether harm reduction programs improved HIV knowledge and stopped risky behaviors among IDUs in Taiwan.
Methods: Harm reduction programs targeting IDUs were implemented in Taiwan in 2005. This study recruited 224 and 283 newly admitted IDU prisoners in 2004 and 2007, respectively. Information on subjects' sociodemographics, HIV knowledge and serostatus, and risky behaviors including needle sharing and cleaning were collected.
Results: The prevalence of HIV decreased by 24.8% for male and by 48.3% for female subjects, two years after the implementation of harm reduction programs. Meanwhile, the percentage of needle sharing among HIV-infected subjects decreased (76.9% in 2004 and 59.5% in 2007). However, subjects in 2007 demonstrated poorer HIV knowledge compared to subjects in 2004. There was no gender differences in HIV knowledge and risky behaviors observed in this study.
Conclusions: Harm reduction implementation including needle exchange program may help prevent risky behaviors and HIV transmission among IDUs in Taiwan. Although IDUs reported decreased risky behaviors, our findings indicated their consecutive lack of HIV knowledge. Findings suggest that prison-based interventions should provide comprehensive health education regarding HIV transmission, prevention, and treatment for imprisoned IDUs.
Financial Support: This study was supported by National Science Council, Taiwan

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COMPARATIVE EFFECTIVENESS AND COST-EFFECTIVENESS OF A COMPUTER-DELIVERED PSYCHOSOCIAL TREATMENT PROGRAM FOR PRISONERS WITH SUBSTANCE USE DISORDERS.

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Aims: 1) To test, among a sample of substance-abusing prisoners, the effectiveness of the Experimental condition (Therapeutic Education System [TES]), a computer-delivered treatment program, versus a control condition (Standard Care—group psychoeducation delivered by a trained clinician), on measures of self-reported drug use, HIV risk behavior, crime and reincarceration; 2) To compare the costs of administering both treatments in a prison setting.
Methods: Employs random assignment to either 1) TES, or 2) Standard Care, in a multi-site trial conducted in 4 States and 10 prisons. This prospective longitudinal study obtains follow-up data post-prison discharge, interviews at 3- and 6-months and criminal record checks to examine the comparative effectiveness of these interventions. Cost data was also collected using a modified version of the Drug Abuse Treatment Cost Analysis Program (DATCAP).
Results: A total of 513 subjects participated in the study (TES N=258; Control N=255). Findings show no significant differences between TES and Standard Care on self-reported outcomes. Rates of incarceration at 12 months post-prison release will be reported. Cost comparisons, however, show that TES was 4-5 times (i.e. cost per client) more expensive to implement in prison when compared to Standard Care.
Conclusions: Results demonstrate the comparative effectiveness of TES and Standard Care. However, TES is 4-5 times more costly to implement. However, this is mainly due to the initial investment required for TES (e.g., license and equipment fees), making the average cost higher when delivered in the context of a short-term clinical trial with limited targeted enrollments. Thus, there are likely to be cost-savings with TES if this technological intervention can be implemented to its fullest capacity. This paper will review the methodological challenges of "scaling-up" costs.
Financial Support: This ongoing ARRA-funded NIDA study, begun in 2009, and is supported by Award Number RC2DA028967.

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EXPOSURE TO STRESSFUL LIFE EVENTS MEDIATES THE RELATION BETWEEN FAMILY HISTORY OF SUBSTANCE ABUSE AND CHILDHOOD ADJUSTMENT.

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Aims: Children with a family history of alcohol and other drug use disorders (FH+) are at increased risk for developing future substance use disorders relative to those without such histories (FH-). The FH+ associated risk is thought to be related to behavioral and emotional maladjustment present prior to the initiation of substance use; however, it is unclear to what extent environmental stressors may be contributing to these deficits. The aim of the present research was to 1) quantify stressful life events in FH+ and FH- children and 2) determine the influence of these events on childhood adjustment.
Methods: Children's self-reported stressful life events and parents' report of their children's emotional and behavioral adjustment were examined in FH+ (n=234) and FH- (n=62) children (ages 10-12).
Results: FH+ children reported significantly more stressful life events than did FH- children; specifically, more instances of abuse, household changes (moving, new people in home), family dysfunction (domestic violence, divorce), academic problems, exposure to crime, and financial problems. Parents of FH+ children also reported significantly higher levels of internalizing and externalizing symptoms in their children. Analyses of the relationships between family history, stressful life events, and child adjustment indicated that stressful life events explained much of the association between FH status and emotional and behavioral adjustment.
Conclusions: FH+ children experience more stressful live events across a broad range of categories, and these stressful life events appear to relate directly to poorer emotional and behavioral adjustment in these children. This research is part of a longitudinal study and the model reported here will be applied to future substance use among these children to determine to what extent stressful life events contribute to problem substance use during adolescence.
Financial Support: National Institutes of Health (R01-DA026868, R01-DA033997)

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OPIOID TREATMENT AND CRIMINAL CHARGES: A COMPARISON OF METHADONE AND BUPRENORPHINE.

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Aims: The aim of this study was to compare the effects on criminal charges of methadone delivered in an opioid treatment program with buprenorphine delivered in primary care.
Methods: We collected demographic and clinical information from chart review for 252 patients initiating buprenorphine and 252 initiating methadone between August 2003 and September 2007. Using the Maryland Judiciary Case Search, we collected data on charges in the two years prior to and two years after initiation. We compared the treatment groups on criminal charges prior to and after initiation, and factors associated with charges after initiation.
Results: There were no significant differences in the number of patients with any charge before or after, or in the number of patients with a drug charge before treatment. After initiation, fewer methadone patients (17.5%) than buprenorphine patients (25.8%) had a drug charge (p=0.02). The methadone group had a lower mean number of drug cases per subject after initiation (0.23±0.55) than the buprenorphine group (0.35±0.70) (p=0.02). In a multivariable analysis of any charges after initiation, cocaine use (OR 1.55 95%CI: 1.01-2.37) and having prior charges (OR 3.29 95%CI: 2.19-4.94) were associated with charges. Having six months of opioid-free urine was negatively associated with charges (OR 0.33 95%CI: 0.22-0.50). In a multivariable analysis of drug charges after initiation, methadone was negatively associated with drug charges (OR 0.55 95%CI: 0.34-0.90) as was prescription drug use (OR 0.40, 95%CI: 0.16-0.99) and six months of opioid-free urine (OR 0.29 95%CI: 0.18-0.48). Having prior drug charges was associated with drug charges after initiation (OR 3.50 95%CI: 2.13-5.74).
Conclusions: While rates of criminal activity and changes over time were similar, methadone may better reduce drug-related crime. Opioid abstinence was strongly associated with not having criminal activity.
Financial Support: Kawasaki: T32 DA026400

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CLINICAL SUPERVISION OF DRUG COUNSELORS IN MALDIVES.

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Aims: To improve effectiveness of drug counseling in the Maldives (estimated up to 30,000 active drug users in a population of 329,000), we implemented and evaluated a clinical supervision training program
Methods: An 8-day workshop on effective drug counseling and clinical supervision skills included lectures, case discussions, and practical exercises. Pre- and post-workshop evaluation surveys evaluated knowledge and attitudes about drug use problems, prevention and recovery, drug counseling, clinical supervision, and self-evaluation of knowledge and professional skills learned during the workshop
Results: Workshop participants were 15 females and 2 males: mean age 30, 12 years of formal education, 6 years of experience working with drug users; highest professional degrees related to counseling included B.A. in psychology (5) and a counseling diploma (12). Differences between pre and post-evaluation results included shifts in the factors identified as the most important for recovery: from internal motivation (endorsed by 15 participants) and family and community support (10 participants endorsed) to availability and accessibility of effective medical treatments (10 endorsements), engagement in psychosocial/behavioral interventions (8), and lifestyle and behavior changes by the recovering individuals (6); and in the clinical supervision skills identified as most important: from a nonjudgmental attitude (11) and empathy (8) to mastery of professional skills by the supervising clinician (10 endorsements)
Conclusions: Workshop participants increased their knowledge and practical expertise of evidence-based interventions, learned about objective evaluation methods, and developed greater appreciation of the importance of delivering goal oriented and structured interventions based on detailed plans, rather than relying on ad hoc, momentary, and subjective judgment of patients' needs or focusing on the motivation of drug users to abstain and the personal characteristics of counselors and supervisors as the most important factors supporting successful recovery. Clinical supervision program in now being implemented in Maldives
Financial Support: European Union

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A NEW GRAPHIC METHOD FOR DATA FROM HUMAN ABUSE POTENTIAL CROSSOVER STUDIES.

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Aims: This presentation proposes a new way of statistical visualization for displaying the data from human abuse potential studies. The human abuse potential study is an important part of the assessment of abuse potential of drugs. This type of study has multiple abuse potential measures and multiple treatments. The study is crossover and often uses a Williams square design. Data are collected for treatments from each treatment sequence and during each treatment period at many time points. This presentation shares the idea of the use of heat maps to display complicated data sets.
Methods: To examine individual data, we use heat maps to display data (3 dimensional or 4 dimensional) from human abuse potential studies. The Williams square is painted using the colors from transparent to very intense based on Emax from individual subjects. The greater the Emax value, the more intense the color. For each measure, we arrange subjects by sequence or by treatment, and use color intensity to show the value of Emax from each subject in each treatment. For each measure, and each treatment, we also use a heat map to display responses from each subject at all time points (constructing time course profiles for individual subjects).
Results: Part of the research has been published in Drug Information Journal. A Graphical User Interface (GUI) in R for heat map displays and other graphical methods that are often used in assessing data from human abuse potential studies has been developed and will be shared within and outside of the FDA.
Conclusions: The heat map display for data from human abuse potential studies provides a tool to visually examine the data. The tool is not restricted to use for Williams square designs. Such heat map displays have wide applicability and could be used for any crossover studies.
Financial Support: This research was supported by funding from the Regulatory Science Review Enhancement Program as well as the Controlled Substance Staff (CSS) at the Center for Drug Evaluation and Research, US Food and Drug Administration.

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TELEVISION WATCHING AND ALCOHOL EXPECTATION ENDORSEMENT THROUGH LATE CHILDHOOD IN TAIWAN.

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Aims: Television is one of channels commonly used to promote alcohol drinks. Children spend more time watching televisions may have greater exposure to alcohol advertisements or TV programs containing alcohol scenes. This study aims to explore the relationship between television watching with change in alcohol expectation endorsement in late childhood.
Methods: Using multistage probability sampling, a prospective cohort of 811 4th grade pupils recruited from 16 public elementary schools in the northern Taiwan in 2007, and followed-up in 5th grade. Information including individual characteristics, family attributes, drinking experiences, and recent television watching time were collected by paper and pencil questionnaires. Alcohol expectancies were assessed via Chinese Alcohol Expectancy Questionnaire-Children version (C-AEQ). Four dimensions selected are on the basis of Cronbach's α (>0.5): "global positive transformation [GPT],""enhanced social behaviors [ESB],""promoting relaxation or tension reduction [PRTR]," and "deteriorated cognitive and behavioral functions [DCBF].
Results: The average of weekly television watching time is estimated 90 minutes. After 9 pm (alcohol advertisement is only allowed to broadcast by regulations), 44.2% and 36.9% children still watched TV in weekdays and weekends, respectively. Total weekly television watching time was not significantly associated with alcohol expectancies (e.g., GPT βwt=0.75, p=0.2), yet watching TV after 9 PM was significantly associated with increased expectation in ESB (βwt=0.49, p=0.02).
Conclusions: Children's positive expectations toward alcohol,especially the dimension of enhanced social behaviors, are related to television watching after 9 PM, . Future research may be needed for possible process and potential implications for prevention and policy should be considered.
Financial Support: National Science Council :NSC95-2314-B-400-009-MY3

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EFFECTS OF DRUG DEPENDENCE ON COMPLICATIONS IN MEDICARE ELDERLY PROSTATE CANCER PATIENTS TREATED WITH PROSTATECTOMY.

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Aims: To analyze the effects of pre-existing substance use on complications in Medicare elderly prostate cancer patients treated with radical prostatectomy.
Methods: We used SEER-Medicare database between 2000-2009 to identify elderly men diagnosed with prostate cancer and treated with radical prostatectomy. We identified those with a pre-existing diagnosis of substance use (ICD-9 codes: Alcohol dependence syndrome-303.xx, Drug dependence 304.xx and Non-dependent abuse of drugs 305.xx). Seven mutually exclusive complications related to radical prostatectomy (respiratory, cardiac, vascular, wound/bleeding, genitourinary, miscellaneous medical and surgical) were identified in the sixty days post-radical prostatectomy. Number of complications is modeled as a factor of pre-existing substance use, after controlling for socio-demographic and clinical characteristics using Poisson regression. We also analyzed the effects of specific types of substance use on complications.
Results: Of the 33,148 men treated with radical prostatectomy, 6.01% had a pre-existing diagnosis of substance use. Complications within sixty days of radical prostatectomy were higher for those with pre-existing substance use (Odds ratio (OR) 1.34; confidence interval (CI) (1.25 to 1.44)), compared to those without. In particular, drug dependence had the highest impact on complications (OR= 4.12; CI=2.86 to 5.94), compared to alcohol and non-dependent abuse of drugs.
Conclusions: Complications related to radical prostatectomy are significantly affected by pre-existing substance use in elderly prostate cancer patients. Also, this affect varies by type of substance use. Complications are an important indicator of quality of care and thus, our results emphasize the need to for early diagnosis and effective treatment of substance use, especially drug dependence, in elderly prostate cancer patients.
Financial Support: Supported by Department of Defense Hypothesis Development Grant, W81XWH-12-1-0089 PC110707

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CHANGES IN PRESCRIPTIONS OF OXYCONTIN AND OPANA AFTER INTRODUCTION OF TAMPER RESISTANT FORMULATIONS AMONG POTENTIALLY PROBLEMATIC AND COMPARATOR PRESCRIBERS.

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Aims: To compare changes in prescription trends in the US for OxyContin® (oxycodone HCl controlled release) and extended release (ER) oxymorphone (Opana) among potentially problematic and comparator prescribers after introduction of reformulations of OxyContin (ORF) (Aug 2010) and Opana (Feb 2012) designed to be more difficult to manipulate for abuse.
Methods: Changes in prescriptions of highest-strength OxyContin (80mg) and OPANA (40mg) were assessed in the period before (Aug 2009 to July 2010) and after (Jan to July 2011) introduction of ORF, and before (Aug 2010 to Jan 2012) and after (Feb 2012 to Sep 2012) reformulated Opana introduction among active prescribers of OxyContin before ORF introduction (≥ 5 OxyContin prescriptions in 5 of 7 months). High dose strengths are preferred for abuse. The analyses compared prescribers who were: 1) prescribers identified through Purdue's Abuse and Diversion Detection (ADD) program as engaging in potentially problematic prescribing behaviors (n=321) and 2) non-ADD prescribers (n=19,744).
Results: After ORF introduction, prescriptions for 80 mg OxyContin declined by 80% in ADD versus 25% in non-ADD prescribers and OxyContin 80mg prescriptions paid by cash declined 98% among ADD versus 83% for non-ADD prescribers. The 321 ADD prescribers accounted for 38% of the decline in 80 mg OxyContin prescriptions in the US after ORF introduction. After ORF introduction, prescriptions for 40 mg Opana increased 391% among ADD prescribers and 112% among non-ADD prescribers. After reformulated Opana introduction, prescriptions for 40 mg Opana decreased 85% among ADD and decreased 55% in non-ADD prescribers.
Conclusions: Prescribers identified a priori with potentially problematic prescribing behaviors showed a significant shift in prescribing following introduction of tamper resistant formulations relative to other prescribers. These findings indicate that a small number of prescribers might account for a substantial portion of diverted prescription opioids, which has important implications for informing policy.
Financial Support: Funded by Purdue Pharma, L.P.

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FRONTAL VS. LIMBIC PREDICTORS OF INHIBITORY SUCCESS IN ADDICTION.

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Aims: Addicted individuals struggle to inhibit their "approach response" to rewarding drugs of abuse, but this battle is often lost. Frontal brain circuits critical for modulating the pull of rewards, and for weighing the potential negative consequences of their pursuit, may be ineffective in many addicted individuals. To capture this brain vulnerability, we tested 1) whether addicted individuals performing a novel Affect-congruent GoNoGo task could activate their frontal circuitry during attempted inhibition, and 2) whether activation in frontal circuits, vs. downstream limbic regions, was a better predictor of inhibitory success/failure.
Methods: Fast event-related BOLD fMRI at 3T (SPM8) was used to measure brain responses in 36 addicted (cocaine, marijuana or prescription opioids) adults during performance of a novel GoNoGo task with pleasant objects that encourage approach (e.g., baby animals) as Go stimuli (87.5% of trials), and dangerous objects that discourage approach (e.g., scorpions) as NoGo stimuli (12.5% of trials). Errors of commission (EoC, failure to inhibit on NoGo trials) were used as the regressor in pre-planned contrasts.
Results: Addicted individuals activated the ventromedial prefrontal cortex and frontal pole during attempted inhibition (peak $t=6.39$; $p<0.005$ uncorr.), but these frontal activations were uncorrelated with task performance (EoC). In contrast, heightened activity in limbic reward-relevant regions (e.g., bilateral ventral striatum/pallidum) during the GO condition significantly predicted inhibitory failure (EoC).
Conclusions: Frontal activations were unrelated to task performance, highlighting the ineffectiveness of frontal modulatory circuits in addiction. Addicted individuals with the strongest limbic activation to positive stimuli had the most difficulty in response inhibition — modeling their real-world struggle to inhibit approach to drug reward, despite potential dangers.
Financial Support: Commonwealth of Pennsylvania CURE Addiction Center of Excellence; NIH/NIDA (T32DA028874; P60DA05186, P5012756); VA VISN 4 MIRECC.

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SYSTEMATIC EVIDENCE REVIEW ON METHADONE HARMS AND COMPARATIVE HARMS.

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Aims: Methadone has come under increasing scrutiny due to data indicating large increases in the number of methadone-associated overdose deaths. The American Pain Society and the College of Problems of Drug Dependence in conjunction with the Heart Rhythm Society commissioned a systematic review of the evidence on the risks associated with methadone and on methods to reduce risks. A multidisciplinary expert panel reviewed the evidence and formulated recommendations based on the review.
Methods: The populations addressed by the evidence review are adults (including pregnant women) and children prescribed methadone for chronic pain or for treatment of opioid dependence. The evidence review assesses evidence on various harms associated with methadone, risk factors for those harms, methods for reducing or mitigating risks associated with the use of methadone, and how the risks of harms associated with methadone are affected by use of concomitant medications.
Results: Investigators reviewed 3,495 potentially relevant citations. Of these, we retrieved 1,107 full-text articles to review for inclusion. After review of full-text articles, we judged 161 studies to be relevant to one or more key questions and to meet inclusion criteria.
Conclusions: The expert panel concluded that measures can be taken to promote safer use of methadone. Recommendations based on the evidence review address patient selection for methadone, patient education, monitoring for QTc prolongation with baseline and follow up electrocardiograms, methadone initiation, monitoring for and management of adverse events, urine drug testing, medication interactions, and methadone use in pregnancy.
Financial Support: The evidence review was conducted at the Oregon Evidence-based Practice Center with funding from the American Pain Society.

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STRAIN DIFFERENCES IN SIGN-TRACKING AND GOAL-TRACKING AS AN INDICATOR OF ABUSE VULNERABILITY IN RATS.

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Aims: Reward-predictive stimuli compel some individuals to approach and interact with the stimulus (sign-tracking), while others approach the location of forthcoming reinforcement delivery (goal-tracking). Using preclinical rat models, a growing literature indicates that individuals that attribute incentive value to a reward-associated stimulus and exhibit sign-tracking behavior, are more likely to initiate cocaine self-administration, expend greater effort for cocaine, and are more susceptible to reinstatement of cocaine-seeking behavior. Additionally, the spontaneously hypertensive rat (SHR), a model of attention-deficit hyperactivity disorder (ADHD), has been shown to exhibit greater drug abuse vulnerability compared to the Wistar Kyoto (WKY). To determine if increased sign-tracking to reward-related stimuli governs the increased abuse vulnerability of SHRs, we utilized a Pavlovian conditioned approach (PCA) task to measure sign- and goal-tracking behavior toward a food-related stimulus in SHR and WKY.
Methods: Six male adolescent SHR and WKY rats underwent 12 sessions of PCA training (8-s stimulus separated by a variable-time 90-s inter-trial interval). Following the PCA task, animals were placed on a modified PCA task for 12 sessions, where any sign or goal tracking during the stimulus resulted in omission of reward.
Results: Mixed-factors ANOVA indicated that SHRs and WKYs exhibited comparable rates of sign-tracking over training, while SHRs exhibited elevated goal-tracking rates. Importantly, SHRs also exhibited elevated goal-tracking rates during the inter-trial interval. Results from the omission sessions indicate that SHRs showed consistent reward omissions, while WKYs showed a decrease in the number of omissions over training.
Conclusions: Collectively, these results indicate, compared to WKYs, SHRs are inattentive and insensitive to the conditioned stimulus during PCA training. Additionally, performance during the omission phase suggests that SHRs are insensitive to consequences, which may mediate the increased drug self-administration in this strain.
Financial Support: NIH grants K99 DA033373, R01 DA12964 and P50 DA05312.

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CHANGES IN MOOD OVER TIME AS A FUNCTION OF EXERCISE AMONG METHAMPHETAMINE-DEPENDENT CLIENTS IN RESIDENTIAL TREATMENT.

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Aims: Mental health status and well-being among individuals dependent on MA continues to be a significant clinical issue during treatment. Clinically, mental health distress among MA abusers in treatment can negatively compound their course of recovery. This abstract provides information regarding a study conducted with MA-dependent users in residential treatment, in part to explore the improvement of mood (depression and anxiety) as a function of exercise.
Methods: Growth curve modeling was conducted to examine mood trajectories over a 1-year period of MA-dependent individuals (n=67) in residential treatment for at least 30 days. Clients were randomly assigned to either 3 days/week of exercise training (n=36) or health education (n=31) over an 8-week study period. Mood was assessed using the BDI and BAI at baseline, weekly, intervention completion (Week 8), and at four follow-up visits. Data presented here are part of an ongoing study.
Results: The average age was 31.5 (SD=7.0); 70.5% were male, and 42% Latino. Results show greater improvements in mental health status over time as a function of the exercise intervention. Growth analyses indicate significant improvements among the exercise participants compared to the education control in depression and anxiety over time, as measured by the BDI and BAI ($p<.05$). Specifically, a significant decrease in depression scores ($B=-2.34$, $p=.043$) and anxiety symptoms ($B=-2.67$, $p<.05$) was observed among the exercise intervention overtime (from baseline to week 26).
Conclusions: Results extend research on treatment evaluations for MA dependence, highlighting the importance of exercise for improved mental health outcomes.
Financial Support: NIDA grant DA027633

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METHYLPHENIDATE DOSE RESPONSE CHARACTERISTICS OF CAUDATE NUCLEUS NEURONAL ACTIVITY CORRELATED WITH ANIMAL BEHAVIOR.

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Aims: To determine if the same chronic dose of methylphenidate (MPD) elicits in one animal behavioral sensitization and in another animal behavioral tolerance. To determine the acute and chronic MPD effect on CN neuronal activity. To determine if there is a correlation between the animals behavioral and CN neuronal firing patterns from animals exhibiting behavioral sensitization to animals exhibiting behavioral tolerance
Methods: Bilateral two electrodes were implanted into each side of the CN. After 5-7 days of recovery and after being habituated to the recording chamber, animals underwent 10 day protocol. At Experimental day 1 (ED1) animals were given a saline injection followed by saline, 0.6, 2.5 or 10.0mg/kg MPD injection and their behavioral and neuronal activity was recorded simultaneously for one hour each. At ED2-ED6 daily injections of MPD were given to elicit a chronic response to the drug. ED7-ED9 was washout days in which no injections were given. At ED10 saline, 0.6, 2.5 or 10.0mg/kg MPD was given, similar to ED1.
Results: Behavioral activity: the acute response of 0.6, 2.5 and 10.0 mg/kg MPD administration elicits dose related excitation of locomotor activity. Chronic MPD exposure, for all doses, elicits in half of the animals behavioral sensitization and in the other behavioral tolerance. Neuronal activity: All acute MPD doses, (0.6, 2.5 and 10mg/kg) elicited mainly excitation of CN units. Chronic MPD exposure at ED10 in the 0.6 elicited attenuation of CN firing rates, while the 2.5 and 10.0mg/kg elicited mainly increases in CN unit activity. Moreover, the CN unit population responses from animals exhibiting behavioral sensitization were statistically different compared to those CN unit population responses from animals exhibiting behavioral tolerance for 2.5 and 10.0mg/kg MPD.
Conclusions: The same dose of chronic MPD can cause behavioral sensitization in one animal and behavioral tolerance in another animals. CN neuronal populations responses of animals exhibiting behavioral sensitization are significantly different from those CN neuronal populations exhibiting behavioral tolerance
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CRACK USE MEDIATES BETWEEN IMPULSIVENESS AND SEX TRADING.

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Aims: The authors hypothesized that crack use mediates the relationship between impulsivity and sex trading, and that this relationship may be different for those who are White versus Non-White.
Methods: Participants were recruited by programs operated by the Center for Behavioral Research and Services (CBRS) at CSU Long Beach. Female (n = 546) participants were administered the Risk Behavior Assessment (RBA) and/or the Risk Behavioral Follow-up Assessment (RBFA) and the Barratt Impulsiveness Scale version 11 (BIS-11). The RBA has questions relating to drug use, incarceration, sexual risk behaviors, and demographics. The BIS-11 overall score was used to assess impulsiveness. Crack use was defined as using crack at least once in the past 30 days, and sex trading was defined as sex trading for money at least once in the last 30 days.
Results: Impulsiveness was related to crack use for Non-whites 95% CI [1.02, 1.07], and for Whites CI [1.00, 1.06]. Impulsiveness was related to sex trading for money for Non-whites 95% CI [1.04, 1.08], and Whites CI [1.04, 1.14]. The meditational model for those who identified as Non-white (n = 375) showed a significant indirect effect (IE) of crack use on impulsiveness and sex trading IE = .11, SE =.03, z = 3.54. However, the meditational model for those who identified as White (n = 171) was not significant IE =.07 SE = 04, z = 1.72.
Conclusions: This study that shows that crack use mediates the relationship between impulsiveness and sex trading, and it furthers our understanding of why women sex trade for money. While this study showed that crack use was a mediator for Non-whites, it is possible that other drugs may mediate the relationship for Whites.
Financial Support: The project was supported in part by Awards R01DA030234 from the National Institute on Drug Abuse, P20MD003942 from the National Institute of Minority Health and Health Disparities, and T34 MH016891 from the National Institute of Mental Health.

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AGE DIFFERENCES IN (±)3,4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA)-INDUCED CONDITIONED TASTE AVERSIONS AND MONOAMINERGIC ACTIVITY.

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Aims: The initiation of drug use in humans generally occurs in adolescence. As such, it is a period of importance in determining factors that play a role in the transition from drug use to abuse. Preclinical work indicates that adolescent rats are more sensitive to the rewarding effects and less sensitive to the aversive effects of abused drugs. The present investigation utilized the conditioned taste aversion design to measure the relative aversive effects of MDMA in adolescent and adult rats.
Methods: Adolescent (PND 21) and adult (PND 78) rats were compared in their ability to acquire taste aversions induced by MDMA (0, 1.0, 1.8 or 3.2 mg/kg). Monoamine and associated metabolite levels in discrete brain regions were also quantified using high-performance liquid chromatography (HPLC) in order to determine if the degree of MDMA-induced aversions was related to MDMA-induced changes in monoamine activity.
Results: Adolescent rats displayed less robust MDMA-induced taste aversions than adult rats during acquisition and on a two-bottle assessment. MDMA at these doses had no consistent dose-dependent effect on monoamine levels, although these levels (and metabolites) did vary with age.
Conclusions: Given that adolescent rats displayed weaker aversions and acquired them at a slower rate than adults suggest that adolescent rats are general insensitive to the aversive effects of MDMA. This relative insensitivity is not a function of differential monoaminergic depletion in that there was no consistent effect of MDMA on monoamine levels. Drug abuse vulnerability is thought to be a function of the balance between the drug's rewarding and aversive effects. The relative insensitivity of adolescents to MDMA's aversive effects may be important to understanding MDMA abuse potential in this specific population.
Financial Support: Supported by a grant from the Mellon Foundation to ALR and generously supported by NIDA, IRP.

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EARLY TREATMENT DRUG USE: DRUG-POSITIVE VS. -NEGATIVE PATIENTS.

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Aims: A positive drug test at start of treatment predicts poor outcomes for stimulant users. But very limited information is available regarding the characteristics of these patients or the significance of early treatment drug use versus abstinence for those with other drug problems. Baseline data from a CTN clinical trial was used to explore these questions.
Methods: Adults (N=494) presenting for outpatient psychosocial counseling treatment at 10 regionally diverse community treatment sites who agreed to participate in a randomized clinical trial of a new web-based psychosocial intervention were classified according to the primary problem drug they identified at treatment entry. Participants were further categorized as positive or negative for their primary drug at study baseline based on: self-reported recent alcohol use (NEG: n=64; POS: n=40) or urinalysis testing of marijuana (NEG: n=37; POS: n=75), cocaine/other stimulants (NEG: n=129; POS: n=41), and opiates (NEG: n=91; POS: n=17). Data collection included demographics, substance use, and 12-step attendance in the last 30 days.
Results: Drug negative and positive subgroups did not differ on demographic variables, but consistent with urine testing data, they differed on self-reported recent drug use. A smaller proportion of alcohol negative (20%) than positive (50%) participants' urine tested positive for one or more secondary drugs. Similarly, 18% of drug negative vs 51% of drug positive cocaine/other stimulants users had evidence of using one or more secondary drugs. Recent 12-step involvement was reported by 69% and 40% of negative vs positive alcohol users and by 74% and 49% of negative vs positive cocaine/other stimulants users.
Conclusions: Early treatment drug abstinence is common across all classes of primary drugs. Those abstaining from their primary drug are less likely to be actively using a secondary drug and more likely to be involved with a 12-step program at treatment entry. These findings suggest individual behavioral differences at treatment start that could inform treatment planning.
Financial Support: NIDA-CTN0044

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ARIPIPRAZOLE FOR THE TREATMENT OF METHAMPHETAMINE DEPENDENCE: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

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Aims: To test aripiprazole for efficacy in decreasing use in methamphetamine-dependent adults, compared to placebo.
Methods: Ninety actively-using, methamphetamine-dependent, sexually active, adults were recruited from community venues.
Participants were randomized to receive 12 weeks of aripiprazole or placebo, with a 3 month follow-up and a platform of weekly 30-minute substance abuse counseling. The primary outcome was regression estimated reductions in weekly methamphetamine-positive urines. Secondary outcomes were study medication adherence (by self-report and medication event monitoring systems [MEMS]), sexual risk behavior, and abstinence from methamphetamine.
Results: Participant mean age was 38.7 years, 87.8% were male, 50.0% white, 18.9% African-American, and 16.7% Latino. Eighty-three percent of follow-up visits and final visits were completed. By intent-to-treat, participants assigned to aripiprazole had similar reductions in methamphetamine-positive urines as participants assigned to placebo (RR 0.88, 95% CI 0.66-1.19, P=0.41). Urine positivity declined from 73% (33/45 participants) to 45% (18/40) in the placebo arm, and from 77% (34/44) to 44% (20/35) in the aripiprazole arm. Adherence by MEMS and self-report was 42% and 74%, respectively, with no significant difference between arms (MEMS P=0.31; self-report P=0.17). Most sexual risk behaviors declined similarly among participants in both arms (all P>0.05). There were no serious adverse events related to study drug, although participants randomized to aripiprazole reported more akathisia, fatigue, and drowsiness (P<0.05).
Conclusions: Compared with placebo, aripiprazole did not significantly reduce methamphetamine use among actively-using, dependent adults.
Financial Support: National Institute on Drug Abuse grant, 1 R01 DA023387-01

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ADOLESCENT RISK-TAKING AMONG BLACK AND WHITE ADOLESCENTS: THE ROLE OF PARENTAL MONITORING AND ENVIRONMENTAL THREATS.

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Aims: Differences in risk taking among Black relative to White adolescents have consistently been reported, suggesting unique mechanisms underlying risk engagement between these groups, which remain unexplored. Specifically, lower rates of substance use has consistently been reported in Black relative to White adolescents. Rooted in Wallace's Racialized Social Systems theory (1999), the influence of parental monitoring, threats in the environment, and their interaction in their relation to risk taking over time were examined. The study was conducted using a laboratory model of risk taking to examine these differences in a controlled setting.
Methods: The sample included 233 adolescents (42% Black) assessed longitudinally across 4 years (between 9 - 16 years old). To evaluate risk taking, we utilized the well-validated BART-Y laboratory risk task (Lejuez et al., 2007). Parental monitoring was measured using an abbreviated version of the Stattin and Kerr (2000) questionnaire. Exposure to threats was assessed through a 21-item scale consisting of self-reported neighborhood, home, and school threats (α's across 4 years = .86-.89).
Results: Hierarchical Linear Modeling analyses indicated that relative to White, Black adolescents engaged in lower risk taking over time (β=-6.69; SE=1.62; p<.001). For Black youths, higher exposure to threats and lower parental monitoring predicted greater risk taking over time (β=—.022; SE=.011; p=.042). However, greater parental monitoring, even in the presence of higher threat exposure, was associated with lower risk taking. The same pattern was not observed in White youths (β=—.013; SE=.019; p=.473).
Conclusions: Results suggest a differential role of environmental factors on risk taking among White and Black adolescents. Future studies should explore additional putative factors that exacerbate or mitigate this relationship.
Financial Support: R01 DA18647

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VALIDATION OF THE GLOBAL APPRAISAL OF INDIVIDUAL NEEDS' GENERAL INDIVIDUAL SEVERITY SCALE AND ITS SUBSCALES AGAINST THE RASCH MEASUREMENT MODEL.

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Aims: The General Individual Severity Scale (GISS) was designed to help clinicians assess severity along four dimensions (substance use, internalizing disorders, externalizing disorders, and crime/violence) and a total general score. Given its wide-spread use by over 3,000 agencies in 48 states and 8 countries, understanding its psychometric properties and, perhaps suggesting ways to improve it, offer a great potential to benefit the field. The aims of this poster are to test the dimensionality and construct validity of the full GISS and its four subscales using the Rasch measurement model and to assess differential scale functioning (DSF) by age and gender.
Methods: Data were collected from 7,435 persons assessed at intake to substance abuse treatment. The sample was predominantly under 18 years of age (73%), male (67%), and Caucasian (45%) or African American (26%). The primary presenting substances were marijuana (49%), alcohol (20.5%), amphetamines (11%), cocaine (11%), opioids (5%), and other drugs (3%).
Results: All the scales were judged to be unidimensional using the proportionality criterion of a 4 to 1 ratio for the variance explained by the principal measure to the variance explained by the first factor of residuals. Each of the four GISS scales exhibited good Rasch person reliability, ranging from .80 to .89. Cronbach's alpha reliability ranged from .90 to .94. Only 4 of 123 items exhibited item misfit using the criterion of >1.33 for both Infit MNSQ and Outfit MNSQ. The criterion-related validity of all scales was consistent with hypotheses. Based on differential test functioning analysis, the full GISS scores had different meanings depending on age and gender of the respondents.
Conclusions: This study supported the use of the four GISS subscales for their target constructs. As suggested by the DSF results, we urge caution in relying only on the GISS total score since variability in how one arrived at a total varied by age and gender.
Financial Support: NIDA grant no. R37 DA011323 and SAMHSA contract no. 270-12-0397.

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VALIDATION OF THE GAIN SELF-HELP INVOLVEMENT SCALE USING THE RASCH MEASUREMENT MODEL.

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Aims: Self-help groups are increasingly recognized as an integral part of managing long term recovery from substance use disorders. The aims of this poster are to evaluate the psychometric properties of the original 21-item Self-Help Involvement Scale (SHIS) and of a short-form version based on traditional measures of internal consistency (e.g., Cronbach's alpha) and the more conservative Rasch measurement model (aka 1 parameter item response theory [IRT]).
Methods: Data were collected using the Global Appraisal of Individual Needs during 2009-2010 from 801 clients in substance abuse treatment who completed the SHIS at 90-days post intake. The sample was predominantly over 18 years of age (71.4%) and male (54%). Over half were Caucasian (54%). Alcohol was reported as a primary drug by slightly over 20%, Marijuana and Opioids were each reported by 18%, Cocaine was reported by 11%, Amphetamines was the least reported primary drug at about 8%. About a quarter were grouped into the other drug category rather than one of five primary drugs listed. Winsteps software was used to place both persons and items on a common, linear, interval "ruler" that enabled examination of: person and item reliability; item hierarchy; item fit statistics; unidimensionality; and item invariance across primary drug of choice.
Results: Both the original and short-form SHIS were internally consistent and met the requirements of the Rasch measurement model except for two items that misfit possibly due to method variance given that these two items had a different rating scale than the remaining items. Item invariance across drugs was observed for 10 items of the full 21-item version. This finding guided selection of items for the short-form version because of our interest in using the measure across primary drug types.
Conclusions: Having available psychometrically sound, full and short-form measures of self-help involvement for use across drugs and treatment types strengthens our ability to discern treatment effects
Financial Support: SAMHSA/CSAT Contract No. 270-12-0397

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BEHAVIORAL AND PHYSIOLOGICAL EFFECTS OF COCAINE SMOKED WITH MARIJUANA.

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Aims: Despite the prevalence of concurrent marijuana (MJ) and cocaine use, there is a paucity of controlled data addressing the interaction between these two drugs. The current study sought to establish the behavioral and physiological effects of cocaine and MJ both when smoked independently and conjunctively.
Methods: Nontreatment-seeking cocaine and MJ smokers were recruited to participate in this within-subject, double-blind, inpatient study. Across 6 laboratory sessions, participants smoked inactive or active MJ (0.0 or 5.6% THC) followed by administration of smoked cocaine (0, 12, or 25 mg). Subjective drug-effect ratings and physiological endpoints were measured throughout the session.
Results: To date, 5 male participants who smoked cocaine (5.2 ± 1.8 days/wk) and MJ (2.9 ± 1.0 days/wk) have completed the study. Active MJ alone significantly increased subjective ratings of marijuana 'Strength' and 'Take Again' relative to inactive MJ ($p \leq .05$). Under inactive MJ conditions, high dose cocaine (25 mg) increased subjective ratings of 'Good Effect,' 'High,' 'Liking,' cocaine craving, and the subjective value of the dose relative to placebo cocaine ($p \leq .05$). Active MJ attenuated cocaine-induced increases in ratings of 'Good Effect,' cocaine craving, and the rated value of the cocaine dose relative to inactive MJ, an effect that trended towards significance ($p \leq .10$). In terms of physiological effects, active MJ increased heart rate relative to placebo, as did 25 mg of cocaine. Active MJ also increased the cardiovascular effects of the low cocaine dose (12 mg) and further increased the effects of 25 mg cocaine on heart rate, an effect that trended towards significance ($p \leq .10$).
Conclusions: These preliminary findings suggest that MJ may decrease the positive subjective effects of smoked cocaine and cocaine craving, while increasing the cardiovascular risk of cocaine. By assessing the interactions between MJ and cocaine, this study will provide clinically relevant information regarding the rationale for why these drugs are co-abused and the health risks associated with the combination.
Financial Support: Supported by NIDA Grants DA027755.

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A SMART PHONE APPLICATION FOR CANNABIS-RELATED PROBLEMS.

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Aims: Despite the prevalence once again increasing, few of those with cannabis use disorder seek specialist addiction treatment. This project aimed to develop and evaluate a smart phone application prior to its evaluation in a randomised controlled trial.
Methods: The methodology included 3 phases. The first was an internet survey of cannabis users, the second phase was an intensively engaged reference group as the app was developed. At the completion of this stage a third group of current cannabis users (n=10), in addition to the reference group, beta tested the app for usability.
Results: The survey of 142 cannabis users (59% male) were aged 12 to 50 years, with the 25-34 year olds making up 36% of the sample. The majority were iPhone users (52%) with 82% having internet connectivity. The majority of these non-treatment seekers (55.6%) found the idea of an app that assists people to monitor and reduce their cannabis use very appealing. The reference group provided feedback on the evolution of the app and the phases of assessing their cannabis use; developing a plan of change; tracking their cannabis use; and tips on coping strategies. The end-user group (60% female) with a mean age of 27 years had never sought treatment for their cannabis use. The majority (71%) enjoyed using the app somewhat or very much and found it very helpful (57%) for evaluating their cannabis use.
Conclusions: The three phase development and testing project demonstrated that cannabis users have access to the required technology and are interested in using an app that would assist them to manage their cannabis use. The next phase of the project will be a small pilot test of the patterns of app use and the impact on cannabis use and related problems to inform the design of a randomised controlled trial. A smart phone app is a promising platform for the delivery of a public health intervention to reduce cannabis use.
Financial Support: The Australian Government Department of Health & Ageing

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USING A NON-INFERIORITY TRIAL APPROACH TO TEST THE HOLISTIC HEALTH FOR HIV (3H+) INTERVENTION AMONG HIV+ DRUG USERS IN TREATMENT.

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Aims: Real world clinical settings such as drug treatment programs are ill-equipped to deploy and sustain the existing - resource-demanding - EBIs that target HIV+ DUs, and this has left a critical void in the overall HIV prevention efforts. In order to address this need, we have conducted formative research in drug treatment settings that has resulted in Holistic Health for HIV (3H+) - an empirically adapted, substantially abbreviated version of HHRP+, a CDC-recommended EBI targeting HIV+ DUs.
Methods: We are conducting a randomized trial comparing the relative efficacy and cost-effectiveness of the brief EBI (3H+) vs. the substantially longer original EBI (HHRP+). Using a non-inferiority approach, we will determine whether 3H+ is comparable (i.e., within a 10% margin) to the original HHRP+ in reducing HIV risk behaviors and improving ART adherence among HIV+ persons in drug treatment who report drug- or sex-related HIV risk behavior.
Results: N/A
Conclusions: If confirmed to be comparable based on the non-inferiority trial model and more cost-effective, as hypothesized, the 3H+ intervention has the potential to be readily and immediately integrated within common clinical settings where large numbers of HIV+ DUs receive clinical services.
Financial Support: NIDA 1R01DA032290 (Copenhaver PI).

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MEDIAL PREFRONTAL CORTEX GRAY MATTER VOLUME IS ASSOCIATED WITH LIFETIME SUBSTANCE USE SEVERITY IN ABSTINENT ADDICTION TREATMENT PATIENTS.

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Aims: Patients with substance use disorders (SUDs) show disruptions in brain function and structure, but the relationship between cortical gray matter (GM) volume and substance use hasn't been established. This study examined the association between cortical GM density and lifetime substance use severity in a sample of recently abstinent SUD patients.
Methods: Subjects (Ss) included 14 predominantly male (64%) and poly-substance dependent (86%) adults aged 26 ± 6 years (range: 19-38 years). Ss were treatment seeking and otherwise healthy. Drug use severity data were collected via Addiction Severity Index and measured as lifetime years of regular substance use. Ss underwent a high-resolution structural MRI brain scan via Siemens Trio 3 Tesla scanner at treatment entry. Image processing and analyses were conducted via optimized voxel-based morphometry implemented in FMRIB Software Library (FSL). Medial frontal GM volume was correlated with reported years of regular substance use using a voxel wise general linear model approach using permutation-based nonparametric testing.
Results: Ss reported a mean of 9 ± 3 years of regular substance use (range: 5-13 years), and were 7 ± 4 days abstinent on the study day (except for nicotine). Bilateral subcallosal medial prefrontal cortex gray matter volume was significantly negatively correlated with reported lifetime years of regular substance use ($p < .05$).
Conclusions: These findings provide preliminary evidence for a relationship between severity of lifetime substance use and cortical structure in SUD patients. Additionally, our results are consistent with the hypothesized link between SUDs and prefrontal cortical disruption.
Financial Support: NIDA K23DA027045, K24DA022288

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GENDER DIFFERENCES IN HIV RISK AND MENTAL HEALTH AMONG METHAMPHETAMINE USERS.

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Aims: This reports results from a study examining gender differences among out-of-treatment, methamphetamine (meth) users. Outcomes included change in HIV risk behaviors, meth use and mental health status.
Methods: Two hundred and fifteen heterosexual meth users were recruited through street outreach in Denver from December 2010 through October 2012.
Results: Of these participants, 52% were women, and 37% were racial minorities. Men and women did not differ in ethnicity, race, marital status, living situation, number of dependents or education. The majority of both men (60%) and women (74%) reported having injected methamphetamine in their lifetimes, and similar percentages of men (9%) and women (8%) reported having either shared needles or used a dirty needle in the past 30 days. When asked about sex exchange, more women (42%) than men (17%) reported having exchanged sex for drugs ($p < .001$), and 40% of women exchanged sex for money (versus 12% of men, $p < .001$). More women (66%) than men (59%) reported having had unprotected sex with a high-risk individual at least one time during the past 30 days, though this difference did not reach statistical significance. High-risk partners included injection drug users, crack smokers, those having sex with multiple persons, HIV+ individuals, and those who the participant either did not know or had just met. On mental health, more women (81%) than men (68%) reported experiencing negative psychological symptoms in the past 30 days ($p < .05$). Reported anxiety was high in this sample among both men and women. Sixty-one percent of men and 71% of women reported experiencing serious anxiety in their lifetime, and 47% of men and 54% of women reported having experienced anxiety in the past 30 days (all ns). Depression was similarly high in this sample, but more women (72%) reported experiencing depression in their lifetimes, than men (58%, $p < .05$). Additionally, women were more likely than men to report having experienced serious thoughts of suicide in their lifetime (52% vs. 39%, $p = .052$) or having made a suicide attempt (40% vs. 24%, $p = .010$). Traumatic experiences are vastly overrepresented in this sample of women. Over eighty percent of women (81%) reported lifetime emotional abuse, 82% reported physical abuse and 63% reported lifetime sexual abuse. By contrast, 61% of men report lifetime emotional abuse, 41% report lifetime physical abuse and 18% report sexual abuse (all $p < .003$).
Conclusions: These findings indicate that female meth users are at high risk for HIV and mental health problems.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA026741.

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THE ASSOCIATION BETWEEN SUBSTANCE USE DISORDER AND RACIAL DISCRIMINATION IN A NATIONALLY REPRESENTATIVE SAMPLE.

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Aims: The purpose of the current study is to determine if racial discrimination is associated with increased substance abuse and dependency in a nationally representative sample. Additionally, the study examined protective factors to reduce the risk of substance use disorder among individuals who experience racial discrimination.
Methods: A cross-sectional study was conducted on the association between chronic discrimination and substance use among a nationally representative sample of African Americans, using the weighted data set from the National Survey of American Life (NSAL). Correlations, means, standard deviations, and ranges were used to examine independent and dependent variables. Bivariate associations between discrimination and substance use disorder within the past 12 months and lifetime were tested using STATA. Multiple logistic regression was used with the dichotomous dependent variables (report of any substance use disorder). Consistent with previous literature, the regression coefficients and standard errors took into account the complex multistage clustered design of the weighted NSAL sample.
Results: Preliminary results suggest a majority of African Americans experience racial discrimination. Racial and other forms of discrimination increase the odds of substance use disorders. Protective factors like inter- and intra-group closelness reduced the odds of substance use problems, whereas a history of arrests, neighborhood crime and drug problems may increase the odds of substance use disorder.
Conclusions: Developing coping strategies for racial discrimination may help to improve substance use disorders among those who experience racial discrimination Reducing racism should be an important consideration for researchers and policy makers. Understanding the prevalence and correlates of discrimination can help addiction researchers and policy makers better understand disparities in substance use disorder duration and outcomes for racial/ethnic minorities.
Financial Support: No financial support.

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INTIMATE PARTNER VIOLENCE VICTIMIZATION AND CIGARETTE SMOKING: A META-ANALYTIC REVIEW.

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Aims: Domestic violence and cigarette smoking both constitute prevalent social problems and are individually associated with significant financial and health consequences. The current meta analytic review represents the first comprehensive empirical evaluation of the strength of the relationship between intimate partner violence (IPV) victimization and cigarette smoking. Demographic and relationship variables were examined as potential moderators of the hypothesized IPV-smoking association.
Methods: Thirty-nine peer reviewed journal articles were detected through database and relevant reference list searches to produce 39 (37 female; 32 physical IPV; 18 pregnant) distinct effect sizes (N=271,192) for use in statistical analyses.
Results: Analyses detected a small to medium composite effect size for the victimization-smoking relationship (d = .41, 95% CI = .35-.47), suggesting that IPV victims were at greater smoking risk than non victims. Subsequent moderator analyses indicated that the association between victimization and smoking is moderately stronger among pregnant compared to non pregnant victims. The strength of the victimization-smoking relationship did not differ by relationship type or ethnicity.
Conclusions: Analyses detected an small to moderate overall association between victimization and smoking with greater risk among pregnant compared to non-pregnant victims. It is recommended that professionals working with IPV victims assess for smoking and offer smoking prevention and cessation skills as appropriate. More research is needed on the smoking behavior of male victims, victims of psychological violence, and victims of ethnic minority status.
Financial Support: This work was supported by the National Institutes of Health grants P50-DA033945 (ORWH & NIDA; PI: Sherry A. McKee, Ph.D.), R03-DA027052 (to AHW), T32-AA007583 (To CAC); Women's Health Research at Yale; the Yale Cancer Center, and the State of Connecticut, Department of Mental Health and Addiction Services.

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SEX DIFFERENCES IN ASSOCIATIONS BETWEEN AGE OF INITIATED CANNABIS USE AND NEUROPSYCHOLOGICAL PERFORMANCE.

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Aims: Earlier initiation of cannabis use is associated with poorer neurocognition across several domains. Given well-documented sex differences in neuromaturation during adolescence, initiation of cannabis use during this time may affect neurocognition differently for males & females. This study examined whether sex moderates associations between age of initiated use (first & regular use) & decision-making (Iowa Gambling Task; IGT), as well as episodic memory (Hopkins Verbal Learning Test-R; HVLT-R).
Methods: Participants were 44 male & 25 female cannabis users aged 18-24 years who were free of several potential premorbid confounds. We conducted moderated hierarchical multiple regression analyses with age of initiated use, sex, & their interaction term entered as predictors. IGT net score, HVLT total immediate, or HVLT total delayed recall scores served as separate dependent variables. All analyses controlled for amount of cumulative lifetime cannabis use to isolate the effects of age of initiated use.
Results: We found an earlier age of first cannabis use, but not regular use, was associated with better decision-making for males & females (β=-.26, p=.04). In contrast, age of regular use was associated with poorer immediate recall for females (β=.28, p=.01), but for not males, & this relationship trended toward significance on delayed recall for females (β=.20, p=.08), but for not males. A similar pattern was observed for age of first use & immediate recall.
Conclusions: Our results provide preliminary evidence that age of initiated cannabis use may have a differential impact on decision-making & episodic memory for males & females. Cannabis use initiated earlier in adolescence may disrupt estrogen-mediated hippocampal development, which may impair memory more in females. Future studies will explore potential factors that may contribute to the unexpected finding of better decision-making among earlier initiators.
Financial Support: NIH grants K23DA023560 & R01DA031176 (Gonzalez), F31DA032244 (Schuster), & P01 CA098262 (Mermelstein).

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PROBLEM BEHAVIORS AND CRIMINAL THINKING AMONG ADOLESCENTS IN RESIDENTIAL SUBSTANCE ABUSE TREATMENT.

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Aims: This study aims to better understand how criminal thinking (Cold-Heartedness, Personal Irresponsibility, and Power Orientation) changes over time in a population of adolescents with varying degrees of problem behavior history. Moffitt's (1993) taxonomy suggests that age interacts with problem behavior history to represent "Life Course Prevalent" and "Adolescent Limited" classifications. We hypothesized that criminal thinking will be higher among young adolescents with more problem behaviors and will change differently depending on drug use severity by each problem behavior history and age group classification.
Methods: Data represent 359 adolescents (53% juvenile justice involved) from 7 residential substance abuse treatment facilities. Clients completed assessments at intake (Time 1) and 35 days (Time 2). Separate 4 (age and behavior history) x 2 (drug use severity) repeated measures ANOVAs were conducted using Personal Irresponsibility (PI) and Power Orientation (PO) as dependent variables. Separate 4 x 2 models were conducted by Gender on Cold-Heartedness (CH) due to preliminary findings indicating higher CH ratings for males than females.
Results: Results indicated a decrease in CH for males with no changes in PI or PO over time. Older females with low drug use severity (regardless of problem history) had higher CH than younger females. Clients with high behavior problems (regardless of age) had higher PI than those with low behavior problems. High drug use severity clients had higher PO than low severity clients.
Conclusions: Problem behavior history and age group classification, gender, and drug use severity were related to specific criminal thinking scales. With the exception of cold-heartedness among males, criminal thinking did not change within the first month of treatment. Findings suggest that criminal thinking can be assessed and interventions can target subgroups of adolescents.
Financial Support: Supported by: NIDA grant R01DA013093.

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LEGAL SUBSTANCE USE AND THE DEVELOPMENT OF A DSM-IV CANNABIS USE DISORDER DURING ADOLESCENCE.

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Aims: To examine whether a) adolescents who initiated use of tobacco or alcohol at an early age are more likely to develop a cannabis use disorder (CUD) during adolescence when compared to non-smokers/drinkers, b) continued use of tobacco or alcohol is related to an increased risk of CUD compared to non-continued use, and c) continued use of both tobacco and alcohol increases the risk to develop CUD compared to single continued use of either tobacco or alcohol.
Methods: We used data from 1584 (54% female) Dutch adolescents who participated in four consecutive assessment waves (mean ages: 11.09, 13.56, 16.27 & 19.20 years) of the TRacking Adolescents' Individual Lives Survey. Age at onset of cannabis abuse or dependence was assessed using the Composite International Diagnostic Interview 3.0. Adolescent tobacco, alcohol and cannabis use were assessed using self-report questionnaires. Cox regression survival analyses were performed.
Results: Early onset tobacco use (HR 2.26; p <0.001), but not early onset alcohol use, increased the likelihood of developing a CUD. Similarly, continued tobacco use, but not continued alcohol use, increased the likelihood of developing a CUD (HR 3.36; p <0.001). Adolescents who combined the use of tobacco and alcohol (both at an early age (HR 1.96; p <0.001) and continuously (HR 3.38 p <0.001) were also more likely to develop a CUD compared to users of either substance.
Conclusions: Early onset use of tobacco, continued use of tobacco, and the combined used of tobacco and alcohol seem to be a more important as a risk factor of CUD when compared to the use of alcohol. Prevention programs should focus on curbing early onset tobacco use as well as the combined use of tobacco and alcohol.
Financial Support: Supported by the Netherlands Organization for Scientific Research (NWO) – Vidi scheme, Netherlands (452-06-004 to ACH and APvL)

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THE IMPACT OF VIVITROL ON SHORT-TERM OUTCOMES POST-MEDICATION.

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Aims: The aims were to examine the effects of Vivitrol (an injectable, long-acting form of Naltrexone) on craving and substance use behaviors once the medication is ceased. Data were collected on urge to drink/use opiates, drug and alcohol use behaviors, client retention, and various treatment outcomes (e.g., engagement, retention, completion).
Methods: The data collected at baseline included the Urge to Drink/Use scale (Urge), the Medication Assisted Treatment Survey (MAT). After the administration of the initial dose, patients completed the Urge and MAT scales every week for the first three weeks and monthly thereafter. All patients had to be simultaneously enrolled in psychosocial treatment at one of the many County-contracted treatment facilities. In addition, at approximately 30 and 60 days after the final dose, patients completed the Urge and MAT scales again. This information was then compared to the data collected while the patient was receiving the medication. At the time of the follow-up, saliva drug tests were also performed.
Results: Preliminary results (n = 50) indicate that although some patient relapse once they are no longer on the medication, many continue with the psychosocial treatment and reportedly remained abstinent. For most patients, cravings or urges did not return to their original levels and for many reported urges remained below the clinically significant threshold – score of 10 on Urge to Drink/Use scale. In addition, saliva drug tests came up negative indicating that patients were able to retain their sobriety.
Conclusions: These preliminary results, although promising do not imply a causal relationship between Vivitrol use and reductions in urges. An additional, perhaps fascinating future research study could examine how urges to drink or use opiates change while a patient is participating in psychosocial treatment compared to those who receive medications in conjunction with just psychosocial treatment.
Financial Support: The Los Angeles County Department of Public Health, Substance Abuse Prevention and Control office supported this research.

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MORPHINE PREVENTS LPS-INDUCED TNF SECRETION IN MAST CELLS BLOCKING IKK ACTIVATION AND SNAP-23 PHOSPHORYLATION. CORRELATION WITH THE FORMATION OF A β-ARRESTIN/TRAF-6 COMPLEX.

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Aims: To investigate the molecular mechanism of morphine-induced suppression of TNF production induced by LPS in mast cells.
Methods: Bone marrow-derived mast cells (BMMCs) were generated by culturing bone marrow from C57BL/6J mice with IL-3 during 4 to 6 weeks. BMMCs were incubated in the presence of distinct concentrations of morphine and LPS-induced TNF production was determined by ELISA. Activated proteins, phosphorylations and molecular complexes were analyzed by western blot, immunoprecipitation and metabolic labeling.
Results: Morphine prevented LPS-induced TNF secretion in BMMCs and that the inhibitory effect was prevented by naloxone. That inhibition was not due to morphine-induced TLR-4 internalization and it was related to the blockage of preformed TNF secretion. LPS-induced TNF exocytosis in BMMCs was dependent on tetanus toxin-insensitive VAMPs and calcium mobilization, as well as PI3K, MAPK and IKK activation. TNF secretion was associated to the phosphorylation of SNAP-23, which forms a complex with IKK in LPS-activated BMMCs. Morphine pre-treatment prevented TLR-4-dependent ERK and IKK phosphorylation. Diminished TAK1 phosphorylation and TRAF-6 ubiquitination was found in BMMCs pre-treated with morphine and stimulated with LPS. Morphine pretreatment provoked a marked increase on the formation of a molecular complex composed by TRAF-6 and β-arrestin 2.
Conclusions: Activation of μ-opioid receptors with morphine suppresses TLR-4-induced TNF release in mast cells preventing the IKK-dependent phosphorylation of SNAP-23 and this inhibition correlates with the formation of a β-arrestin 2/TRAF-6 complex.
Financial Support: Supported by Conacyt (grant 188565 to CGE and scholarship 200394 to IKMS).

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ROLE OF THE NORADRENERGIC LOCUS COERULEUS COMPLEX IN MEMORY FORMATION UNDERLYING RELAPSE.

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Aims: These experiments were designed to characterize the role of neurochemical systems in the transition from abstinence to relapse, and aid the development of pharmacotherapeutic agents targeted towards relapse prevention. Specifically, we hypothesized that noradrenergic (NA) cell groups in the locus coeruleus (LC) complex would be involved in the memory formation process underlying relapse.
Methods: We used a reacquisition procedure in rats involving: habituation, place conditioning (1 mg/kg heroin), a test of conditioning (Test I), extinction, a test of extinction (Test II), reconditioning (1 mg/kg heroin) and test of reconditioning (Test III). Rats received systemic (0, 10, 40, 100 ug/kg) or bilateral intra-LC clonidine (aCSF, 4.5, 18 nmol), an α2-receptor agonist, following heroin reconditioning. To verify that intra-LC clonidine reduced NA activity, we stained for c-fos and measured expression in LC projection sites (i.e. basolateral and central amygdala; BLA and CeA). Rats received bilateral aCSF or unilateral aCSF, and in the opposite hemisphere, unilateral clonidine (4.5, 18 nmol) 90 min prior to being sacrificed.
Results: ANOVAs were used. We found that 10 and 40 ug/kg of clonidine blocked heroin reacquisition when given right after (n=13, 12) or 4h (n=12, 18) post reconditioning, but 40 ug/kg had no effect 8h (n=6) post reconditioning or when given 4h (n=5) before Test III. Similarly, intra-LC clonidine (18 nmol) blocked reacquisition when infused immediately (n=8) or 4h (n=10) post reconditioning, but had no effect when given 4h before (n=8) Test III. Consistent with these results, BLA and CeA c-fos activity was reduced only after 18 nmol clonidine (n=5). No effects on reacquisition or c-fos activity were observed when clonidine was administered into adjacent regions.
Conclusions: These data suggest that reacquisition of drug-place associations involves a memory process sensitive to manipulations of the NA LC complex. We propose a novel preclinical use of clonidine as a pharmacological treatment for relapse prevention.
Financial Support: Supported by NSERC.

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ONLINE INTEREST IN SYNTHETIC MARIJUANA AND POLICY IMPLICATIONS.

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Aims: Synthetic marijuana is a varied set of synthetic cannabinoids, sprayed on organic materials and then smoked. Toxicology results indicate the level of cannabinoids to be 100-800 times higher than in natural marijuana. Often marketed as a "legal high", these products are growing in popularity among young people. The aim of this study was to examine the interest in synthetic marijuana in the U. S. using standard online search methodology as a proxy for interest; and to determine the availability of websites offering to sell synthetic marijuana online.
Methods: Using the same tools online advertisers use for marketing, appropriate "search terms" were constructed to mimic terms that might be used by a young person searching for synthetic marijuana. Next, we surveyed Internet websites for the most prevalent search term—herbal incense. Two independent raters examined the links generated in each search conducted during Nov-Dec 2011 and resolved coding disagreements. The resulting links were coded as "retail", "information", or "other" (usually news sites). On January 1, 2012, we queried Google Insights for Search and Google Trends with "herbal incense" as the search term and examined the trends nationally and by state from 2008 through 2011.
Results: "Herbal Incense" is the most common search term used to search for synthetic marijuana and yielded over 2 million search results in Google annually. The top 10 retail sites yielded 142,579 unique U.S. visitors monthly. Of the first 100 unique websites, 87% were retail, 4% were information, and 9% other. We observed a reduction in the number of online searches within states with strict legal sanctions and no change in states with less comprehensive legal sanctions.
Conclusions: Synthetic marijuana warrants greater policy consideration. Marketed as a "legal high", this form of marijuana is widely available online. We discuss how the Internet complicates enforcement of legal sanctions. One limitation of this study is that we were not able to measure actual rates of purchase.
Financial Support: No financial support.

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BLOCKADE OF N-METHYL-D-ASPARTATE RECEPTORS IN THE NUCLEUS ACCUMBENS SHELL INCREASED NICOTINE SELF-ADMINISTRATION BUT HAD NO EFFECT ON NICOTINE-INDUCED CONDITIONED TASTE AVERSION.

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Aims: Nicotine increases glutamate transmission in mesolimbic brain sites such as the ventral tegmental area (VTA) and the nucleus accumbens (NAcc). This nicotine-induced increase in glutamate transmission partially mediates the reinforcing effects of nicotine. Direct injections of the competitive N-methyl-D-aspartate (NMDA) receptor antagonist, LY235959, into the VTA attenuated the reinforcing effects of nicotine. However little is known about the role of NAcc shell NMDA receptor-mediated glutamatergic transmission in the reinforcing effects of nicotine.
Methods: In the present study, the effects of bilateral administration of LY235959 (0, 0.1, 1 & 10 ng/side) into the NAcc shell were evaluated on intravenous nicotine self-administration (fixed- and progressive-ratio schedules) and food self-administration (fixed-ratio schedule) in rats. Furthermore, the effects of LY235959 in the NAcc shell on the aversive effects of nicotine were assessed using nicotine-induced conditioned taste aversion in rats.
Results: LY235959 injections (10 ng/0.5µl/side) into the NAcc shell compared with saline increased nicotine self-administration under both fixed- ($n = 8$; $p < 0.01$) and progressive-ratio schedules ($n = 7$; $p < 0.05$), decreased food self-administration ($n=8$; $p < 0.01$), and had no effect on nicotine-induced conditioned taste aversion.
Conclusions: Taken together, these data suggest that blockade of NMDA receptor-mediated glutamatergic neurotransmission in the NAcc shell increases the reinforcing and motivational effects of nicotine without any influence on the aversive effects of nicotine. Furthermore, the effects of the NMDA receptor antagonist on food self-administration suggest that NMDA-mediated glutamatergic neurotransmission is required for food-maintained operant responding. Overall, the results suggest that NMDA-mediated glutamatergic transmission in the NAcc shell negatively regulates the reinforcing and motivational effects of nicotine.
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SPATIAL AND NEIGHBORHOOD-LEVEL CORRELATES OF RETENTION IN PHARMACOLOGIC EFFICACY TRIALS.

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Aims: Many studies have described individual-level correlates of substance use treatment retention; however, few studies have examined the role of ecologic factors in participant retention. We sought to assess the relationship between structural factors such as spatial and neighborhood-level characteristics with participant retention among actively-using methamphetamine-dependent individuals in pharmacotherapy trials.
Methods: Retention data, pooled from three pharmacologic trials (cumulative sample=180), was defined as "high" by completion of at least 85% of weekly study visits during a 3-month follow-up period and "low", otherwise. Using residential address at enrollment, we calculated distance (miles) to study visit site as well as measures for neighborhood accessibility using walkscore.com. Participants who did not provide data on residential address (n=16) were excluded. Data were mapped by neighborhood using ArcGIS and differences were assessed using Fisher-exact and Wilcoxon ranksum tests.
Results: Overall mean retention rate was 83% (SD=25.8). High retention participants were more likely to live at closer distances (mean=3.0 miles [SD=8.4] versus mean=6.4 [12.6]; $p =0.01$) and were more likely to reside in locations with greater neighborhood accessibility (mean=91.7 walkscore [SD=14.2] versus mean=87.3 [16.2]; $p=0.02$), compared to low retention participants. Results were consistent in subgroup analyses among participants of color and those age 40 and over ($p<0.05$).
Conclusions: We found that high retention was significantly associated with closer distance from the treatment site and better neighborhood accessibility. These results suggest that pharmacologic substance use trials should consider structural factors, such as spatial and neighborhood-level factors, and interventions to reduce spatial barriers to participation in efforts to maximize retention.
Financial Support: This study was funded by the National Institute on Drug Abuse (R01-DA022155; R01 DA023387-01, R21 DA021090).

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DOSE-RESPONSE CHARACTERISTICS OF NUCLEUS ACCUMBENS NEURONS AS ASSESSED BASED ON THE ANIMALS BEHAVIORAL RESPONSE TO CHRONIC METHYLPHENIDATE TREATMENT.

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Aims: The same dose of methylphenidate (MPD) elicits behavioral sensitization or tolerance. This study determined if the same dose elicits both behavioral sensitization and tolerance, by recording the NAc neuronal activity following acute and chronic MPD simultaneously with the animals behavior.
Methods: Electrodes were implanted into the NAc, neuronal and behavioral activity was recorded simultaneously. At Experimental day 1 (ED1) animals were given a saline injection followed by 60min recording followed by saline, 0.6, 2.5 or 10.0mg/kg MPD injection and their behavioral and neuronal activity resumed for one hour. At ED2-ED6 daily injections of MPD were given to elicit a chronic response to the drug. ED7-ED9 were washout days. At ED10 recordings were resumed following a saline, 0.6, 2.5 or 10.0mg/kg MPD.
Results: Behavioral activity: the acute response of 0.6, 2.5 and 10.0 mg/kg MPD administration elicits dose related excitation of locomotor activity. Chronic MPD exposure elicits to half of the animals behavioral sensitization and to the others behavioral tolerance for all doses. The neuronal population following 0.6 and 2.5mg/kg MPD recorded from animals expressing behavioral sensitization exhibit significant ($p<0.02$) difference in response pattern from animals expressing behavioral tolerance, while following 10.0mg/kg MPD no differences were observed. The acute 0.6 mg/kg MPD predominately elicited an attenuation of NAc firing rates, while the 2.5 and 10mg/kg MPD in NAc units elicited mainly excitation. Following chronic MPD exposure, (0.6, 2.5 and 10.0mg/kg) at ED10 in animals expressing behavioral sensitization an increase in their firing rates was predominately. Animals that exhibited behavioral tolerance a decrease in activity was predominate.
Conclusions: The same dose of MPD can cause behavioral sensitization in one animal and behavioral tolerance in another. The NAc neuronal population recorded from animals exhibiting behavioral sensitization are significantly different from those exhibiting behavioral tolerance
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INDIVIDUAL DIFFERENCES IN NEGATIVE URGENCY BEHAVIOR: RELATIONSHIP WITH DOPAMINE TRANSPORTER FUNCTION.

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Aims: Negative urgency is a facet of impulsivity and refers to a tendency to engage in rash action when experiencing negative emotion. Individual differences in urgency predict drug abuse. Dopamine (DA) system dysregulation in amygdala, prefrontal cortex and nucleus accumbens have been implicated in impulsive behavior, but little is known about the neural mechanisms of negative urgency. Extracellular DA levels depend on presynaptic release and uptake processes. The current study tested the hypothesis that DA transporter (DAT) function is an important mechanism underlying individual differences in negative urgency and drug abuse vulnerability. The current study evaluated the relationship between individual differences in DAT function in striatum, nucleus accumbens, medial prefrontal cortex (mPFC) and orbitofrontal cortex (OFC) and negative urgency using an animal model
Methods: Male Sprague Dawley rats (n=24) were tested for negative urgency behavior using an operant task employing 3 test sessions, each including 24 reward trials and 8 omission trials. Increased responding during omission trials relative to reward trials was defined as negative urgency. Brain regions of interest from each rat were used for kinetic analyses of [3H]DA uptake (DAT function) to obtain Km and Vmax and parameter values were correlated with behavioral measures
Results: Results showed that negative urgency was positively correlated (Pearson correlation $r=0.531$, $p<0.05$) with Vmax in nucleus accumbens, but not in striatum, mPFC or OFC.
Conclusions: Thus, results confirm that omission of reward engenders greater operant responding and extends previous work by showing that increases in negative urgency behavior are associated with increases in DAT function in nucleus accumbens. Increased DAT function is expected to result in reduced concentrations of extracellular DA in accumbens. Thus, dopaminergic hypoactivity in nucleus accumbens may mediate individual differences in negative urgency.
Financial Support: NIH P50 DA05312

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A COMPARISON OF LONG-TERM TREATMENT OUTCOMES FOR COCAINE DEPENDENCE: ABSTINENCE, HOMELESSNESS, AND EMPLOYMENT.

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Aims: Abstinence, homelessness, and employment outcomes of enhanced groups from three randomized controlled trials treating cocaine dependent homeless, H2, H3 and H4 (combined n=542) were compared. Enhanced groups received abstinence contingent housing and work therapy (ACH/WT) and behavioral day treatment, while controls lacked a component in subsequent dismantling designs aimed to increase treatment effectiveness. In H2 (DT+) and in H3 (ACH) received ACH, while controls did not. In H4, (CM+) received behavioral day treatment, while its control (CM) did not. DT+, ACH, and CM+ groups all received work therapy, but in H3 work therapy was not abstinence contingent for ACH. We hypothesized the H4 enhanced group would have better outcomes than H2 and H3 groups.
Methods: Abstinence was measured by urine toxicology with consecutive weeks abstinent (CWA) baseline to 12 month follow-up as the outcome, homelessness was measured by self-reported days housed within the last 60 days at 12 months, and employment by reported days worked within the last 60 at 12 months. For each outcome, a one-way ANOVA tested for group differences.
Results: Differences were found between groups on abstinence ([F (2, 539) =40.304, p=0.000]) and housing [F (2, 397) =6.032, p=0.003]) outcomes, but not for days employed where means were 26.5, 22.9 and 28.1 days for H2, H3 & H4. Follow-up tests revealed differences in CWA between DT+ and CM+ (6.38 vs 12.19 weeks p=0.000) and ACH and CM+ (6.39 vs 12.19 weeks p=0.000), and differences in days housed between DT+ and ACH (35.10 vs 23.35 days p=0.005) and ACH and CM+ (23.35 vs 32.40 days p=0.017).
Conclusions: Differences in abstinence suggests improved treatment effectiveness over subsequent trials. That both DT+ and CM+ had better homelessness outcomes than ACH suggests the abstinence contingent work therapy, incorporated in DT+ and CM+, but not a component of ACH, was more effective for sustaining housing.
Financial Support: Partially supported by NIDA grant R01 DA11789-04, RTI International and UAB

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DEVELOPMENT AND EVALUATION OF THE MARIJUANA REDUCTION STRATEGIES SELF-EFFICACY SCALE.

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Aims: Develop and evaluate key psychometric properties of a self-report questionnaire designed to assess young regular marijuana users' self-efficacy to employ 21 different strategies intended to reduce the amount, frequency and/or speed with which they consume marijuana.
Methods: Following approval of the project by our institutional review board, we sent an email during the spring semester, 2012, to a random sample of 8,000 undergraduate students enrolled at a large public Midwestern university asking them to consider participating in an online survey asking about their use of marijuana. 273 regular marijuana users rated their confidence that they could employ each of the strategies. Additionally, they completed measures assessing their problems with marijuana and other substances, refusal self-efficacy, marijuana use history, and motives for using marijuana.
Results: Based on principal components analysis, internal consistency reliability, and mean inter-item correlation, we retained all 21 items in a single scale. This evaluation supported several elements of convergent and criterion validity; specifically, self-efficacy to reduce marijuana use scores were significantly positively correlated with refusal self-efficacy, and significantly negatively correlated with quantity and frequency of marijuana use, marijuana-related problems, and several motives for using marijuana.
Conclusions: This relatively short and easily-administered questionnaire could be used to identify marijuana users who have low self-efficacy to employ specific marijuana reduction strategies and as an outcome measure to evaluate educational and skill-training interventions designed to increase one's confidence that they could employ protective behavioral strategies to reduce their use of marijuana.
Financial Support: There was minimal (less than $200) financial support provided by the psychology department at BGSU.

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PYROLYSIS STUDIES OF SYNTHETIC CANNABINOIDS IN HERBAL PRODUCTS.

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Aims: To determine the chemical fate and biological exposures that occur during the smoking of synthetic cannabinoids in herbal formulations through the characterization of the chemical composition and delivery (yields) of mainstream smoke constituents.
Methods: Herbal cigarettes laced with synthetic cannabinoids such as JWH-018, JWH-250 and AM-2201 were prepared and smoked using a Borgwaldt KC smoking machine. The smoke condensate was collected, dissolved in solvent and analyzed using a Waters Synapt 2 Q-TOF-MS and an Agilent 7001B triple quad GC/MS. Samples were analyzed against standard material and blank cigarette smoke to confirm identity and determine recovery. Mass defect filtering and precursor ion searching allowed us to identify likely pyrolysis products in the chromatograms. We identified a number of active pyrolytic products in the smoke of hand-rolled synthetic cannabinoid cigarettes by LC/MS. GC/MS was used to confirm the identity of the parent and pyrolysis compounds found.
Results: Precursor ion searching based on the 127 ion of AM-2201 smoke indicated that at least 5 pyrolysis degradation products, including JWH-018, JWH-022 and three other compounds had been formed. Precursor ion search of JWH-018 smoke showed JWH-022 as a degradation product (loss of 2 hydrogens). JWH-167 was also formed during the pyrolysis of JWH-250 (loss of methoxy group).
Conclusions: Synthetic cannabinoids degrade to other products when smoked. These pyrolysis products can be components that have an altered affinity to the CB1 and CB2 receptor, or entities of unknown pharmacology and toxicology.
Financial Support: This work was funded by RTI International as an internal research and development project.

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ADULT ADHD SUBTYPES, AUTISTIC TRAITS, AND SUBSTANCE USE.

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Aims: Individuals with Attention-Deficit/Hyperactivity Disorder (ADHD) are more likely to report
substance use but few studies have investigated this relationship within ADHD subtypes. ADHD symptoms and Autism Spectrum Disorder (ASD) traits tend to co-aggregate, but the combined effect of ADHD and ASD traits on substance use is not understood. This study examines the occurrence of substance use in ADHD subtypes and the relationship between ADHD,ASD,and substance use
Methods: Subjects were 3273 young adults between the ages of 18-39 years with available parent-report data from a population-based study of Missouri large sibship families.They were classified as inattentive (ADHD-I), hyperactive-impulsive (ADHD-HI), combined (ADHD-C) or unaffected based on application of the DSM-IV ADHD symptom criterion to parent-report SWAN (Strengths and Weaknesses of ADHD-symptoms and Normal behavior) questionnaire responses. Substance use (tobacco, alcohol, and drugs) and ASD trait data were derived from the ABCL (Adult Behavior Checklist) and SRS (Social Responsiveness Scale). Group differences in mean T-scores were assessed using clustered linear regression and appropriate post-hoc tests. SRS score of 65 or higher was defined as above-threshold ASD traits
Results: Adults with ADHD used substances more frequently compared to controls, and the ADHD-C subgroup showed significantly higher use than other subtypes (i.e., mean T-scores for the frequency of tobacco use statistically differed across ADHD groups as follows: ADHD-I=53.87, ADHD-HI=55.14, ADHD-C=58.87, Controls=51.47). In subjects with ADHD, high ASD traits further increased risk for frequent substance use. For instance, excessive drinking was reported in 24% of individuals with ADHD plus high ASD traits, compared to 10% with ADHD but low ASD traits, 5% with high ASD traits but no ADHD, and 3% with neither ADHD nor high ASD traits
Conclusions: Individuals with ADHD (especially combined subtype) are vulnerable to frequent use of alcohol, tobacco and drugs. Elevated ASD traits, when they co-aggregate with ADHD, further increase this vulnerability
Financial Support: MH-083823
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A BRIEF BEHAVIORAL TELEHEALTH INTERVENTION FOR VETERANS WITH ALCOHOL MISUSE PROBLEMS IN VA PRIMARY CARE.

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Aims: Alcohol misuse disorders are prevalent among veterans and the availability of effective treatments in primary care is a significant health care need. The aim of this study is to present preliminary treatment outcome data based on the self-reports of 11 VA primary care patients with alcohol misuse disorders who completed a brief telehealth intervention, based on motivational interviewing and cognitive behavioral therapy (BIAM-PC; Santa Ana, 2010), regarding their average and peak amount of alcohol consumption.
Methods: This project is a prospective within-subject repeated measures design with 1 treatment group, BIAM-PC, delivered to a total of 25 primary care patients who identified as having an alcohol misuse disorder using validated assessment instruments. Participants were evaluated at three time points (pre-, post-treatment, and at 2-month follow-up). Four individual therapy sessions were delivered in the participant's home via 1-hour one-on-one video-conferencing sessions over a 4-week period.
Results: Paired samples t-tests indicate a significant reduction ($t=-2.63$, $p<.05$) in participants' reported Standard Ethanol Content (SEC) from baseline (M=124.13, S.D.=101.48) to the 2-month follow up (M=48.21, S.D.=46.43). Also, a significant reduction in peak SEC scores ($t=-3.74$, $p<.01$) was found (baseline M=17.04, S.D.=8.63, 2-month follow up M=4.86, S.D.=4.88). These data suggest that BIAM-PC is associated with reductions in average and peak alcohol consumption in primarily alcohol dependent veterans.
Conclusions: These preliminary findings suggest that the BIAM-PC intervention may prove effective in reducing harmful or hazardous drinking behavior in veterans who present to primary care. Results are part of a larger study evaluating feasibility of BIAM-PC.
Financial Support: This project was supported by the South Carolina Clinical & Translational Research (SCTR) Institute with an academic home at the Medical University of South Carolina CTSA, NIH/NCRR Grant Number UL1RR029882. The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH or NCRR.

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INITIATION INTO DRUG DEALING AMONG STREET-INVOLVED YOUTH IN A CANADIAN SETTING.

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Aims: Drug dealing is a risky activity common among street-involved youth in many urban settings. While participation in illicit drug markets is associated with violence and a range of drug-related harms, little attention has been given to factors that may be associated with initiation into drug dealing among street-involved youth. We sought to identify demographic, economic, and drug use factors associated with initiation into drug dealing and hypothesized that specific drug use patterns would predict entry into drug dealing among this vulnerable population of youth.
Methods: Data for this longitudinal analysis were derived from the At-Risk Youth Study (ARYS), a NIDA funded prospective cohort of street-involved youth aged 14 to 26 in Vancouver, Canada. Cox proportional hazards regression was used to identify factors independently associated with time to drug dealing initiation.
Results: Between September 2005 and May 2012, 1006 participants were recruited into ARYS and 768 (76%) had a history of drug dealing at baseline. Among the 238 participants with no history of drug dealing, 157 returned for study-follow-up and where included in our analysis. Over study follow-up we observed 46 drug dealing initiation events, for an incidence density of 15.2 per 100 person-years. Factors that were independently associated with drug dealing initiation in multivariate Cox regression were: younger age (Relative Hazard [RH]= 1.3, 95% CI: 1.1-1.50), male gender (RH= 2.4, 95% CI: 1.2-4.5), recent crystal methamphetamine use (RH= 3.5, 95% CI: 1.9-6.3) and recent crack cocaine smoking (RH= 4.0, 95% CI: 2.1–7.4).
Conclusions: These findings highlight that drug dealing is extremely prevalent among street-involved youth and indicate that stimulant drug use is a key risk factor for drug dealing initiation among this population. Innovative stimulant addiction treatment and economic empowerment interventions for street-youth may help prevent drug dealing among this high-risk population.
Financial Support: US NIH (R01DA028532) and CIHR (MOP–102742)

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ABUSE OF OXYCONTIN® AND IMMEDIATE-RELEASE OXYCODONE IN A RURAL KENTUCKY COUNTY FOLLOWING INTRODUCTION OF REFORMULATED OXYCONTIN: RESULTS FROM 6-MONTH FOLLOW-UP INTERVIEWS.

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Aims: In August 2010, shipments of original OxyContin (oxycodone HCl controlled-release; OC) stopped and reformulated OxyContin (ORF) started. OxyContin was reformulated to render it more difficult to manipulate for the purposes of intentional abuse. This study describes changes in abuse 1-2 years after ORF introduction among individuals who had abused OC in rural Kentucky.
Methods: Structured follow-up interviews assessing opioid use were conducted in 164 individuals who abused OC, 85% of the original sample of individuals interviewed about pre- and post-ORF drug use (n=192). Participants reported retrospectively about abuse, including past 30-day use via any route (days/month), in interviews conducted January 2011-April 2012, approximately 6 months after the initial interview.
Results: Most participants (76%) selected OC as their preferred drug prior to ORF introduction; (66%) selected immediate release (IR) oxycodone as their preferred drug after ORF introduction. From the initial post-ORF interview to 6-month follow-up, the prevalence and frequency (days/month) of OC abuse declined (60% to 11% and 11.3 to 3.3 days/month among those who abused, respectively). During the same time period, prevalence of ORF abuse declined (33% to 18%); among those who were abusing ORF, frequency remained stable (5.9 vs. 5.7 days/month). At follow-up, 23% reported attempting to manipulate ORF for purposes of abuse, though only 1 participant selected ORF as the preferred drug. There was a decline in the prevalence of any IR oxycodone abuse (96% to 85%); the frequency among those abusing IR oxycodone remained relatively constant.
Conclusions: OxyContin changed from being the preferred drug for the majority of abusers before ORF introduction to the preferred drug for <1% of abusers at follow up, while the prevalence of OC abuse declined due to decreased availability. There was a shift in preference from OC to IR oxycodone as availability of OC declined.
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THE NATURAL HISTORY OF ADOLESCENT BINGE DRINKING: FINDINGS FROM A 15-YEAR PROSPECTIVE COHORT STUDY.

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Aims: We examined the natural history of adolescent "binge" and "heavy binge" drinking from adolescence to young adulthood; and which characteristics of predict the continuity of "binge" and "heavy binge" alcohol use into young adulthood.
Methods: A 15-year prospective cohort study in Victoria, Australia comprising 1943 adolescents recruited from secondary schools at age 14-15 years. Levels of past-week "binge" drinking (5+ standard drinks (SD) on a day, each 10g alcohol) and "heavy binge" drinking (20+ SD on a day for males, 11+ for females) were assessed during six adolescent waves, and across three adult waves up to the age of 29 years.
Results: Half of males (52%) and a third of females (34%) reported past-week binge drinking in adolescence. Most adolescent-onset binge drinkers (nine in ten male and seven in ten females) continued to binge drink into young adulthood. Seventy percent of males and 48% of females who were not adolescent-onset binge drinkers reported binge drinking in young adulthood. Past-week "heavy binge drinking", reported by 19% of males and 15% females in adolescence, increased substantially in the young adult waves (38% males, 27% females at any adult wave). There was some evidence of a decline at 29 years. Among adolescent binge drinkers (n=821), being male, adolescent antisocial behaviour, and adverse consequences of drinking in adolescence predicted adult bingeing.
Conclusions: Alcohol is a major preventable cause of disease burden. Given that heavy consumption in young people in many countries has become the norm, and continuity into young adulthood high, these findings suggest that alcohol related deaths and disability among young people are set to continue to rise in many countries.
Financial Support: Funding provided by Australian Rotary Health and the NHMRC. NDARC is supported by funding from the Australian Government.

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THE INFLUENCE OF AGE AND GENDER ON THE LIKELIHOOD OF ENDORSING CANNABIS USE DISORDER CRITERIA.

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Aims: Cannabis users aged 18-24 years have a higher prevalence rate of cannabis use disorders (CUD) than older cannabis users. Because the development of the CUD criteria was largely based on adult populations, these differences in prevalence rates might result from differential item functioning in adolescents and young adults. Although findings from previous research focusing on CUD criteria demonstrate measurement bias across age as well as gender, no study to date has simultaneously examined the influence of age and gender on the likelihood of endorsement of the various CUD criteria.
Methods: The sample consisted of 8,172 adult lifetime cannabis users participating in an American population study (16.6% aged 18-24; 46.0% women). Cannabis use and past year CUD criteria (DSM-IV) were assessed with the AUDADIS-IV. A Restricted Factor Analysis with Latent Moderated Structures was used to detect measurement bias.
Results: All CUD criteria were significantly more prevalent in younger (18-24) versus older (24-89) cannabis users (chi-square ranging from 70.69 – 521.77), and – with the exception of Role impairment and Withdrawal – in men versus women (chi-square ranging from 4.91 – 17.42). With regard to measurement bias, age group did not affect the likelihood of endorsing any of the CUD criteria. Only the criterion Legal problems showed gender related measurement bias, with men being more likely than women to endorse this criterion (beta = -0.34).
Conclusions: The results indicate that CUD criteria function similarly across age groups, but show gender related measurement bias for Legal problems. This supports the application of the CUD-criteria across different age groups, and supports the necessity to change the criterion Legal problems in DSM-5.
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TELEPSYCHIATRY FOR PATIENTS WITH CO-MORBID PSYCHIATRIC AND SUBSTANCE USE DISORDERS: A UCLA INTEGRATED SUBSTANCE ABUSE PROGRAMS (ISAP) AND LOS ANGELES COUNTY DEPARTMENT OF PUBLIC HEALTH–SUBSTANCE ABUSE, PREVENTION, AND CONTROL (SAPC) PILOT.

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Aims: The aim of the UCLA ISAP/SAPC telepsychiatry pilot is to provide psychiatric services via telemedicine to patients admitted to the LA County operated Antelope Valley Rehabilitation Center (AVRC) located in rural Acton, CA.
Methods: All patients in this project were diagnosed with a DSM-IV-R SUD plus significant psychiatric co-morbidity, but did not have a severe and persistent mental illness (SPMI).The UCLA ISAP psychiatrist provided services to patients one day a week using a secure, web-based, mobile telemedicine cart and accompanying software. Using a low-cost medication formulary, the psychiatrist prescribed psychotropic medications for a number of issues including depression and anxiety.
Results: Over 100 unique clients have been seen; most have had multiple follow-up sessions. Client outcomes were examined using County admission and discharge and a brief survey assessed patient satisfaction. Outcomes data for discharged patients indicate that individuals participating in the project reported decreases in substance use, increases in mental illness diagnoses, and increases in medication prescription for mental illness. Additional outcomes will be compared to similar non-pilot patients. Results of the patient satisfaction survey indicate that patients were satisfied with the quality of care, the sound quality, the picture quality, and felt that their mental health needs were being met.
Conclusions: This project has been well-received by patients and staff. It demonstrates that telepsychiatry in a rural SUD inpatient facility is feasible. In conjunction with a low-cost formulary and increased medication management, it is possible to incorporate telepsychiatry services in rural inpatient SUD treatment.
Financial Support: This research was supported by Los Angeles County Department of Public Health–Substance Abuse, Prevention, and Control.

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EVALUATED IRON IN THE GLOBUS PALLIDUS OF METHAMPHETAMINE USERS: MRI SUSCEPTIBILITY IMAGING.

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Aims: Preclinical studies consistently demonstrated that methamphetamine (MA) administration may hasten age-related brain degeneration. Young adult rats exposed MA showed similar neurochemical profiles as aging rats, and young vervet monkeys who received only two doses of MA (2mg/kg i.m.) had iron levels similar to levels of aging monkeys in the substantia nigra and basal ganglia. The levels of iron concentration in deep subcortical structures, such as the basal ganglia, may lead to magnetic susceptibility variation that can be noninvasively measured by frequency shift using susceptibility MRI.
Methods: Ten subjects were studied: six chronic MA-dependent subjects (age=44.5±3.5 years, MA use duration=17.4±3.4 years, daily used=1.0±1.2 grams) and four non-drug user controls (age=47.0±2.8 years). MRI data were acquired on a Siemens 3T TimTrio scanner using a Gradient-echo sequence (TE/TR=30/3500ms, resolution=0.4x0.4x2.0mm). The acquired phase data were unwrapped, and the phase contribution from non-brain structure such as air-tissue interface was removed. For group comparison, phase images from individual subjects were registered to a MNI 1mm brain template for analyses in the same brain regions.
Results: : The frequency shift in the globus pallidus of MA users (1.52±0.16 Hz) were higher than those in the controls (1.18±0.18 Hz), p=0.03. However, the values in the putamen and caudate were not significantly different between the two groups. Age-dependent increase in frequency shift was found in MA users only (r=0.35, p=0.017), but the slope was not different from the controls.
Conclusions: Chronic MA users had higher frequency shift that likely reflect higher levels of iron concentration in the globus pallidus. These findings are consistent with those observed in the MA-treated young vervet monkeys, and suggest that MA use may lead to accelerated aging especially to the dopaminergic system. Ongoing studies will evaluate group differences in age-dependent changes in brain iron levels.
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CORRELATION BETWEEN SEVERITY OF ADDICTION AND LEVEL OF SERVICES RECEIVED BY ALCOHOL USE DISORDER OUTPATIENTS IN FRANCE.

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Aims: Studies have shown that matching level of care to patient baseline severity improved treatment outcome. The aim of this study was to examine the correlations between severity of addiction and the level of care received by alcohol use disorder outpatients in France.
Methods: Consecutive patients from 8 nationwide alcohol addiction treatment outpatient clinics were asked to participate in the study. After informed consent, participants completed a baseline-structured interview that included the Addiction Severity Index (ASI) modified to include tobacco, and the Treatment Service Review (TSR). The ASI and the TSR were repeated at 3, 6 and 12-month follow-ups. The correlations between the severity of addiction (ASI severity score) and the level of treatment received (number of contacts reported in the TSR) were calculated by Spearman's ρ.
Results: 100 patients were included (74% males, 47.9 y.o.). They mostly exhibited impairment in the Alcohol, Psychiatric, Employment, Family/Social, Tobacco and Medical domains of the ASI. No significant correlation with the level of care was found. Patients received the same level of care for alcohol regardless of baseline severity. Half of those who required psychiatric care did not receive it, and 50% of those with low severity scores in the Medical domain of the ASI received somatic care. Only a minority (4%) received tobacco-related care whereas 85% of patients required such care.
Conclusions: In this sample, the level of care was not individualized to the level of severity. Clinicians seemed to apply the same treatment protocol to every patient regardless of individual baseline severity of addiction. An algorithm for better allocating patients to treatment might be helpful and cost-effective.
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COMPARING THE ABILITY OF MULTIPLE MEASURES OF SUBSTANCE ABUSE TREATMENT PROCESS TO PREDICT OUTCOMES.

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Aims: To compare the ability of multiple treatment process measures (individual or in combination) to improve our ability to predict outcomes relative to traditional length of stay measure.
Methods: Participants were 274 adults in the Early Re-intervention (ERI) experiment (51% female, 80% were African American, average age of 39.5 years). The 11 individual process measures included: length of stay from records, treatment satisfaction, treatment received, and the substance abuse treatment index from the Global Appraisal of Individual Needs (GAIN); treatment participation and peer support from Client Evaluation of Self and Treatment (CEST); and impulsivity-maturity, social skills, accepting program philosophy, program engagement, and attachment and investment from the Client Activity Inventory (CAI). Combinations of measures were created based on the total variance represented by an effect indicator model. Outcomes included GAIN scales related to substance frequency, substance related problems, recovery environment risk, social risk and employment.
Results: Each measure was related to outcomes, combinations of measures by source (i.e. From GAIN, CEST, CAI) did better than any individual measures, and the combination of all 11 measures did better than by those by source. However, the combination of just 3 measures (GAIN substance treatment index, the CEST treatment participation scale and the CAI attachment and investment scale) did the best.
Conclusions: The results suggest that treatment processes scales are better able to predict outcomes than length of stay and that combinations of them are better. However most of the improvement comes from a subset of three measures – which actually do better than all 11 combined. This study suggests that future process research needs to cluster patients on needs and then examine the relationship of their services to outcomes.
Financial Support: The National Institute on Drug Abuse Grant number R37 DA11323

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BIDIRECTIONAL CHANGES IN REWARD RESPONSIVENESS DURING NICOTINE WITHDRAWAL AND ACUTE NICOTINE ADMINISTRATION ASSESSED IN THE RESPONSE BIAS PROBABILISTIC REWARD TASK IN RATS.

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Aims: Deficits in reward processing are hypothesized to play an important role in relapse amongst abstinent smokers. The aim of the present study was to determine the effects of nicotine withdrawal and subsequent nicotine exposure on reward responsiveness in rats. Reward responsiveness (i.e., the propensity to modulate behavior as a function of prior reinforcement experience) was assessed using a translational behavioral task originally developed for humans and recently adapted for rats.
Methods: Male Wistar rats (n=34) were trained to discriminate two tones varying in duration in operant boxes for food pellets. During test sessions, one tone (rich) was reinforced three times more frequently than the other tone. Rats were tested after 24 hr spontaneous withdrawal from either nicotine (6.32 mg/kg/day, base) or saline delivered for 28 days via subcutaneous osmotic minipumps. The effects of acute nicotine (0, 0.125, 0.25, 0.5 mg/kg, base, sc) were assessed in the same rats between 2 and 8 weeks after termination of chronic nicotine administration using a Latin-square design.
Results: Saline-treated rats developed a response bias towards the rich stimulus, while response bias was significantly decreased during nicotine withdrawal, reflecting diminished reward responsiveness. Acute nicotine administration (0.25, 0.5 mg/kg) potentiated response bias in rats previously exposed to chronic nicotine compared to saline-treated rats, reflecting enhanced reward responsiveness by acute nicotine in rats with previous nicotine experience.
Conclusions: Decreased reward responsiveness during nicotine withdrawal and the enhancement of reward responsiveness by acute nicotine in rats with chronic nicotine exposure and withdrawal could potentially play an important role in relapse in abstinent smokers. Thus, treatment of deficits in reward responsiveness in abstinent smokers may facilitate smoking cessation.
Financial Support: NIH Grants: MH078979 (DAP and AM), DA011946 (AM)

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GENDER DIFFERENCES IN WITHDRAWAL WHEN USING VERY LOW NICOTINE CONTENT CIGARETTES.

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Aims: The effect of very low nicotine content (VLNC) cigarettes on withdrawal in men and women were examined. Women report more withdrawal than men in select cessation studies. However, the difference may be partly due to greater sensitivity to nonpharmacological aspects of smoking in women, which remain intact with VLNC cigarettes.
Methods: As part of a larger study (Hatsukami et al., 2010), treatment-seeking smokers (N=46) smoked 0.05 mg nicotine yield cigarettes for 6 weeks before making a quit attempt. Weekly changes in withdrawal symptoms, assessed by the Minnesota Nicotine Withdrawal Scale, relative to baseline were examined using latent growth curve models. Change in withdrawal symptoms one week post-quit attempt was examined using multiple regression.
Results: On average, withdrawal symptoms increased after switching to VLNC cigarettes (intercept = 2.13, p = .004) but returned to baseline levels within 3 weeks (slope = -.90, p = .004) with little change thereafter (slope = -.08, p = .72). Withdrawal differed by gender, controlling for baseline smoking and withdrawal, and age. Women had greater initial withdrawal than men (p = .005), particularly irritability, depression, anxiety, and restlessness. Within three weeks, withdrawal was similar across genders due to a faster decreasing rate of symptoms during that period in women. The gender effects may not result from different smoking rates, because there were no gender differences of initial VLNC cigarette smoking levels (p = .76) and changes in smoking levels did not predict initial withdrawal symptoms (p = .15). Following a quit attempt, on average, there was no significant increase of withdrawal symptoms (p = .46) and severity did not differ across genders (p = .15).
Conclusions: Women experience more withdrawal, particularly negative affect, after switching to VLNC cigarettes than men even though their smoking rates are similar. Additional research is needed to replicate these findings with larger sample sizes.
Financial Support: P50 DA013333; U54 DA031659

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RETENTION OF PARTICIPANTS IN OPIATE SUBSTITUTION PROGRAMS IN LOW AND MIDDLE-INCOME COUNTRIES: AN INTERNATIONAL SYSTEMATIC REVIEW.

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Aims: Opiate substitution therapy (OST) is a key component in overdose prevention, reducing illicit opiate use and risky blood borne virus infection. By retaining participants in OST programs for longer periods of time, more noticeable and permanent changes in drug use, risk behavior, and quality of life can be achieved. There have been many studies documenting retention in OST programs among high-income countries, establishing a 50% 12-month follow-up retention rate as a marker for a successful OST program. However, we do not have a systematic understanding of how successful programs have been in retaining participants in low and middle-income countries (LMIC) over time.
Methods: Utilizing PRISMA guidelines we conducted a systematic literature search to obtain studies that documented changes in retention, over time, for participants in buprenorphine and methadone programs in low and middle-income countries. Retention was measured for participants by length of follow-up, type of OST pharmacologic treatment, and treatment dosage
Results: Overall retention after 12 months was 54%. Pooled retention was moderately good for both buprenorphine (48.3%) and methadone (56.6%), after 12 months of treatment. Among studies utilizing methadone, there was no statistically significant difference in retention by dosage level, and the ten highest and lowest dosage studies obtained similar retention levels (47% vs. 49%) after 12 months.
Conclusions: The results of this review demonstrate that even with limited resources, LMIC have successfully achieved the 50% retention minimum among OST participants after 12 months, and retention in LMIC is comparable to those seen in established OST programs in high-income countries. Due to the infancy of many of these programs, it is important to monitor progress in the early years to ensure continued retention success for future participants and future established programs.
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NEGATIVE AFFECT, EMOTIONAL AWARENESS AND SUBSTANCE USE IN ADOLESCENTS AND YOUNG ADULTS.

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Aims: The current study investigated associations between negative affect, emotional awareness and substance use (alcohol, cigarettes and marijuana) in newly parenting adolescents and young adults.
Methods: Participants were young females (mean age = 18.7) and their male partners (mean age = 21.3; 421 total participants) recruited from obstetrics and gynecology clinics in Connecticut. Negative affect was assessed via symptoms of depression and stress using the Center for Epidemiological Studies-Depression Scale and the Perceived Stress Scale. Emotional awareness was assessed using the Emotional Expression Scale for Children, and substance use in the past three months was assessed using single items.
Results: Generalized estimating equation models showed a significant main effect of emotional awareness on alcohol, cigarette and marijuana use during the past three months, such that less emotional awareness was associated with higher odds of substance use after adjusting for negative affect. Emotional awareness also significantly moderated associations between depressive symptoms and alcohol use; for those with greater emotional awareness, higher levels of depressive symptoms were associated with higher odds of alcohol use. Additionally, gender moderated the association between emotional awareness and cigarette use ($p < .06$); less emotional awareness was associated with greater odds of cigarette use among females than males.
Conclusions: Findings suggest complexity in associations between emotional awareness, negative affect and substance use, including potential gender differences. Higher emotional awareness may play an important role in protecting against substance use overall, but may also operate as a vulnerability factor for alcohol use in those with depressive symptoms. Findings may inform refinement of interventions to prevent substance use and abuse among newly parenting adolescents and young adults.
Financial Support: This study was supported by a NIMH grant (1R01MH75685) and a NIDA grant (T32 DA019426).

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EYE-TRACKING MEASURES OF ATTENTIONAL BIAS IN COCAINE-DEPENDENT SUBJECTS.

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Aims: Cocaine-dependent subjects show evidence of attentional bias toward cocaine-related cues, and this measure of cue-reactivity is predictive of craving and relapse. Cue-reactivity and attentional bias have been assessed by a variety of models that feature presentation of drug-relevant stimuli (e.g. cocaine Stroop task) and measurement of reactivity (e.g. heart rate, reaction times). In the present project, we developed a novel attentional-bias task using eye-tracking based measurement of saccadic eye movements towards cocaine and neutral cues. Previous studies have indicated competition between the higher-order cortical processes (frontal eye-fields, DLPFC) in voluntary eye control (i.e. anti-saccades) and more reflexive saccades driven by involuntary midbrain (superior colliculus) perceptual input (i.e. pro-saccades).
Methods: Cocaine-dependent subjects and healthy controls are tested using eye-tracking technology to measure performance on counterbalanced blocks of pro-saccade and anti-saccade trials featuring cocaine and neutral stimuli (pictures). Dependent measures include anti-saccade errors, saccadic response times and latencies, and pupil diameter during fixation on stimuli.
Results: Preliminary analysis of the eye-tracking data in 22 completed subjects (13 cocaine, 9 control) indicate higher attentional bias in cocaine dependent subjects as measured by anti-saccade errors (i.e., looking toward the stimulus), both across all stimuli (35% vs. 26% anti-saccade errors), and specifically in the presence of cocaine-related stimuli (41% vs. 22% anti-saccade errors).
Conclusions: We expect to complete testing on 60 subjects (30 per group) by June 2013. We hypothesize that, relative to controls, cocaine dependent subjects will exhibit greater anti-saccade errors, longer reaction time latencies, and greater pupil diameter (during fixation) on cocaine-stimulus trials. This novel saccade-based measure of attentional bias is expected to provide a rich method by which to assess reactivity to drug cues and eventually to screen for potential relapse prevention interventions.
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HERITABILITY OF CANNABIS AND TOBACCO USE INITIATION: FINDINGS FROM A GENETICALLY INFORMATIVE FEMALE TWIN COHORT.

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Aims: The prevalence and incidence of lifetime cannabis use is especially high among those with a lifetime history of tobacco smoking and genetic factors contribute to their co-occurrence. We examined the extent to which variation in – and covariation between – age of initiation of marijuana and regular tobacco smoking is attributable to heritable factors, as well as shared and non-shared environmental factors.
Methods: Multivariate genetic models were fitted to diagnostic data obtained from a population-based, prospective cohort of 3787 female twins aged 18-27 years at the time of interview. Onset of regular tobacco-use was defined as at least 1 cigarette daily, and onset cannabis-use was defined as usage at least once during lifetime.
Results: Approximately 43% of the sample reported lifetime cannabis use, with mean onset age of 16.61 years (SD=2.62). Approximately 36% had smoked regularly (mean age=18.11, SD=2.38). Age at initiation of cannabis use and regular smoking was correlated (r=0.39). The magnitude of heritable versus non-shared environmental variation in tobacco smoking age of onset approximated 38% and 65%, respectively, whereas the magnitude of heritable variation in cannabis use age of onset approximated 38%, with the remaining variance attributable to shared (24%) and non-shared (38%) environmental factors. Whereas the genetic overlap in age of onset for tobacco and cannabis-use was substantial (78%), overlap in non-shared environmental variance was negligible (6%). Thus, 60% of the covariation between initiation of cannabis use and regular tobacco use was due to additive genetic factors.
Conclusions: Overlapping genetic influences linking cannabis and tobacco use play a role as early as initiation of use. Future analyses will explore whether after accounting for this genetic overlap, age at onset of marijuana and nicotine dependence are also influenced by common genetic factors.
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MDMA USE IS ASSOCIATED WITH LOWER GRAY MATTER VOLUME IN WIDESPREAD CORTICAL REGIONS.

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Aims: MDMA has been a popular recreational drug for 25 years and is now in trials as an adjunct to psychotherapy. Animal models show serotonergic neurotoxicity at high doses, while human studies suggest that recreational exposure is associated with lower serotonin signaling and long-term cognitive changes. Studies investigating the association of MDMA use with brain gray matter volume have been equivocal, with evidence for lower brain gray matter in MDMA users as well as with evidence for no difference in gray matter volume in MDMA users.
Methods: We recruited 41 MDMA users (mean 31.3 lifetime MDMA episodes) and 30 non-users aged 18-34 and abstinent from recreational drugs (excluding nicotine and caffeine) for at least two weeks. Gray matter, white matter and CSF volume were measured using structural cranial MRI scans pre-processed with DARTEL and analyzed using the voxel based morphometry (VBM) method in SPM8, controlling for total intracranial volume.
Results: Lifetime MDMA use was negatively associated with gray matter volume in bilateral regions of the frontal, temporal, parietal, occipital and limbic lobes (correlation coefficients ranged from -0.6 to -0.8), with no regions featuring a positive association. Although MDMA users had greater polydrug use than the control group, the association between MDMA use and lower gray matter volume remained after controlling for lifetime use of other drugs. In the between-group analysis, MDMA users had lower gray matter volume throughout the cerebrum. Regional white matter volume was also negatively associated with lifetime MDMA use and was lower in the MDMA group. Over the entire brain, the ratio of gray and white matter volume to total intracranial volume was 3.5% lower in MDMA users.
Conclusions: Recreational use of MDMA is associated with lower cortical gray matter volume. Further research is needed to determine the functional consequences of lower gray matter volume and whether these differences in brain structure pre-exist MDMA use or result from MDMA exposure.
Financial Support: R01DA01537, R21 DA020149, K01MH083052, UL1RR024975

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CIRCADIAN DISRUPTION INCREASES METHAMPHETAMINE CONSUMPTION IN METHAMPHETAMINE-DEPENDENT RATS.

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Aims: A substantial number of clinical studies indicate associations between circadian rhythm abnormalities and drug abuse; however, the role played by the circadian system in the development of addiction is largely unknown. The goal of this study was to examine the effect of experimentally induced circadian disruption on oral methamphetamine consumption in rats.
Methods: Male Sprague-Dawley rats (n=32) were housed in running wheel cages in a 12:12 light:dark cycle. Feeding, drinking, and locomotor activity were continuously recorded. Methamphetamine dependence was induced in one group of rats (n=16, dependent) with two weeks of forced methamphetamine consumption (0.01% in drinking water) while a second group (n=16, drug naïve) received water only. This was followed by a two week abstinence period during which half of the animals from each group were exposed to 4 consecutive 6-hr advancing phase shifts of the light:dark cycle, while the other half remained on the original light:dark cycle. In all rats, methamphetamine consumption following the deprivation period was assessed using a two-bottle choice paradigm.
Results: As would be predicted due to the development of sensitization, methamphetamine consumption was initially decreased in dependent vs. drug naïve rats. However, consumption escalated more rapidly and remained significantly higher in phase-shifted rats of the dependent group compared to all other groups.
Conclusions: These data reveal a robust effect of circadian rhythm disturbance on dependence–induced increases in methamphetamine consumption, and suggest that dysregulation of the circadian system be considered in the etiology of relapse and addiction.
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EXTERNAL VALIDATION OF THE POTENTIAL CONCERN INDEX MODEL BASED ON INDIVIDUAL PRESCRIBING PATTERNS.

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Aims: We reported preliminary findings from a genetic algorithm that created a Potential Concern Index (PCI) from analysis of various aspects of individual prescribing at CPDD (2011). We revisited those prescribers with the top 100 PCIs to learn if the PCIs computed previously predicted the likelihood of subsequent problems, such as board of medical examiners (BOMEX) actions and arrests.
Methods: Data from 2007-2008 for ~500,000 opioid prescribers were analyzed previously to generate a listing rank-ordered by PCI. Internet sites of news media, BOMEX, and other sources were searched in 3Q12 to determine whether individual prescribers with the highest PCIs had undergone administrative or legal actions.
Results: No information was found on 3 and 6 were deceased. Twenty-four of the top 100 had active licensure with no readily-available evidence of BOMEX or law enforcement action. Of the 67 remaining, 46 had licensure actions in force (15 revocations, 10 surrenders, 7 suspensions, 14 active with restrictions/conditions). Another 17 had undergone administrative actions or arrests, listed by action and (licensure status): 7 current BOMEX complaints (active); 7 prior BOMEX actions (restored to active); 1 BOMEX action taken (inactive); 1 arrested (active); 1arrested (inactive). Suspicious media reports (eg, patient deaths, office raided by police) were found for 4 prescribers with currently-active licensure.
Conclusions: This analysis provides support for the potential of this model in prospectively identifying prescribers whose patterns suggest concerns to public safety. By focusing on empirically-derived lists of prescribers, law enforcement and BOMEX investigators could rule out prescribers practicing competently, identify prescribers in need of remediation, and intervene on criminal activity earlier than is typical by spontaneous complaints and delayed follow up. Earlier intervention with high-risk prescribers, whether educational or enforcement-related, would save lives and money.
Financial Support: Supported by Principled Strategies and Purdue Pharma L.P.

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EXAMINING PERCEIVED COERCION AMONG INCARCERATED SUBSTANCE ABUSERS PARTICIPATING IN RESEARCH.

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Aims: The growing nexus of drug dependence and crime has increased the need for effective interventions for substance abusing offenders, resulting in a proliferation of studies to evaluate their efficacy. Substance abusing offenders represent a doubly vulnerable population with regard to making informed decisions about research participation. Despite federal requirements to ensure the autonomy of research participants, there are no measures designed to identify specific sources of real or imagined coercion in this population. We developed the Coercion Assessment Scale (CAS; Dugosh, et al., 2010) to identify specific coercive pressures that substance abusing offenders may experience when asked to participate in research. In the current study, we examined rates of perceived coercion in a sample of incarcerated substance abusers participating in an ongoing NIH-funded study.
Methods: A total of 64 incarcerated substance abusers enrolled in a biomedical trial were recruited for participation. Participants completed the 15-item CAS within one month of recruitment into the parent study. Descriptive statistics were calculated to examine the prevalence of different perceived sources of coercion in this sample.
Results: Rates of perceived coercion were generally low. Approximately 19% of participants felt that the judge would like it if they entered the study and 6% felt that entering the study would help their case. In addition, about 6% of participants felt their parole officer would like it if they entered the study. Overall, 20% of participants identified at least once source of perceived coercion.
Conclusions: These findings support the use of the CAS in studies involving incarcerated substance abusers who are participating in research. In this context, it can help to identify individuals who may need enhanced consent procedures or who may not be appropriate for study participation. Identifying real or imagined sources of coercion would allow researchers to correct misperceptions or address actual coercive influences.
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YOU STARTED SMOKING WEED WHEN YOU WERE HOW OLD?

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Aims: There has been much debate on the effect of alcohol and tobacco use on marijuana use among youth. This study examines the effect of the prevalence and age of initiation of tobacco and alcohol use on the age of initiation of marijuana use among youth in California, Georgia, Michigan, New York, and Texas.
Methods: The sample includes data from 1991-2011 from the Youth Risk Behavior Survey. A two part Probit model, using SAS genmod procedures, was used to estimate the separate effects of marijuana use in last 30 days and the age of initiation of marijuana use in the last 30 days and lifetime. Prevalence and age of initiation of alcohol and tobacco use were used as predictors.
Results: Youth who smoked cigarettes (OR 13.71, $p<0.0001$), drank alcohol (OR 9.75, $p<0.0001$), or smoked cigarettes and drank alcohol (OR 2.03, $p<0.0001$) in the last 30 days had higher odds of last 30 day marijuana use. Youth in California, Michigan, and New York had statistically significantly higher odds of last 30 day marijuana use as compared to youth in Georgia. Younger age of initiation of cigarette and alcohol use was associated with higher odds of younger age of initiation of last 30 day (cigarette: OR 1.41, $p<0.0001$; alcohol: OR 1.24, $p<0.0001$) and lifetime marijuana use (cigarette: OR 1.38, $p<0.0001$; alcohol: OR 1.24, $p<0.0001$). Youth in California and Michigan had statistically significantly lower odds of younger age of initiation of marijuana use in the last 30 days and lifetime, respectively, as compared to youth in Georgia.
Conclusions: This work has the potential to inform the policy community on the usefulness of surveillance to understand how patterns of drug use among youth differ by State and can be helpful for planning youth-focused substance use prevention and treatment services.
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CHRONIC PAIN AND COPING STRATEGIES WITHIN METHADONE AND BUPRENORPHINE-MAINTAINED PATIENTS.

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Aims: There is a high prevalence of chronic pain in methadone-maintained (MM) patients and no one has examined chronic pain among buprenorphine-maintained (BM) patients.
Methods: This study examines the prevalence, severity, and frequency of chronic pain, coping strategies, and comorbid disorders in MM and BM patients using a confidential and anonymous survey (n=92).
Results: Data were compared as a function of chronic pain (CP). Fifty-four percent of patients endorsed pain and 48% of those endorsed CP. Compared to non-CP, CP patients reported more past year utilization of physicians (p=.01) and emergency rooms (, p<.01). CP patients also reported greater ratings of average pain (p<.01) and pain right now (p=.02); higher ratings of pain interference with general activity (p=.03) and walking ability (p=.04); and greater ratings on the McGill Pain Questionnaire-Short Form sensory (p<.01) and affective subscales (p=.02). CP patients had higher ratings on the Coping Strategies Questionnaire (p=.04), though no differences in use of other coping strategies (e.g., medications, prayer) were reported. CP patients also had higher scores on the Pain Catastrophizing total scale (p=.02), and rumination (p=.02), and helplessness (p=.05) subscales, and a greater prevalence of concurrent medical disorders (p<.01). No differences in demographics or drug use, acute withdrawal symptoms, psychiatric problems, or sleep disturbance were reported, suggesting the groups did not vary on dimensions commonly associated with heightened pain perception.
Conclusions: These data indicate a large percentage of MM and BM patients experience chronic pain that is interfering with their daily life. Patients are choosing high cost medical services over numerous potential coping strategies, which highlights a potential area for intervention. Ultimately, these data provide a comprehensive characterization of pain that will lead to the development of strategies to reduce and better manage pain in MM and BM populations.
Financial Support: NIDA T32 DA007209, K24 DA023186

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WOMEN WHO TRADE SEX FOR DRUGS ONLY AS A HIGH-RISK SUBGROUP OF SEX WORKERS: AN EXPLORATORY ANALYSIS.

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Aims: To compare levels of HIV risk behavior and infection among African American women who trade sex for drugs only, those who trade sex for money (and also may have traded sex for drugs), and those who have no reported history of sex trade.
Methods: A secondary data analysis of African American women (N = 254; M age = 36.5, SD=8.9) enrolled in a NIDA-funded NEURO-HIV Epidemiologic study in Baltimore, Maryland. Participants were recruited via street outreach, advertisements, and participant referral. Participants completed a face-to-face psychosocial interview, including questions about demographics, drug use, sex trade and other risk behaviors. Blood was drawn to test for HIV infection.
Results: Of the 254 African American women in the sample, 77 (30.3%) had a history of trading sex for money or for money and drugs, 15 (5.9%) had a history of trading sex for drugs only, and 162 (63.8%) had no prior history of sex trade. Three (20%) participants who traded sex for drugs only tested positive for HIV compared to four (5.2%) who traded sex for money and drugs. This difference was significant (X2(1, n=92)=3.92, p=.048). Women with no prior sex trade were also more likely to be HIV positive (14.9%) than women who traded sex for both money and drugs (X2(1, n=239)=4.67, p=.031) but had comparable HIV rates to those who traded sex for drugs only (p=0.598). On average, women who had a history of trading sex for drugs only reported using condoms during just over one-quarter of sex acts in their lifetime (M=28.0, SD=30.6), while women who traded sex for money or money and drugs reported using a condom nearly half of lifetime sex acts (M=46.7, SD=27.1) (t(90)=2.39, p=.019). Furthermore, those who trade sex for drugs and are HIV positive reported only 6.6% condom use.
Conclusions: Implications of this study suggest that African American women who trade sex for drugs may represent an understudied, yet elevated HIV risk group with heightened rates of HIV possibly due to lower condom use rates.
Financial Support: This research was funded by NIDA R01 DA14498.

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STRUCTURAL MODIFICATIONS TO TETRAHYDROPYRIDINE-3-CARBOXYLATE ESTERS TOWARDS THE DISCOVERY OF M5-PREFERRING MUSCARINIC RECEPTOR ANTAGONISTS AS NOVEL TREATMENTS FOR DRUG ABUSE.

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Aims: The M5 muscarinic acetylcholine receptor (mAChR) is the current pharmacotherapeutic target for discovery of treatments for drug abuse.
Methods: A series of M5-preferring antagonists was designed based on a 1,2,5,6-tetrahydropyridine-3-carboxylic acid scaffold. Inhibition of [3H]N-methyl-scopolamine binding to membranes from Chinese hamster ovary cells individually expressing human hM1-hM5 mAChR served as the initial screen. Inhibition of oxotremorine-induced [3H]dopamine release from rat striatal slices evaluated activity of M5 selective compounds. A homology model of human M5 mAChR, based on the newly available crystal structure of rat M3 with antagonist tiotropium bound, was constructed and docking studies performed to understand the binding mode of the novel compounds.
Results: Compounds 28 and 56 had high affinity (Ki = 230 nM) and modest affinity (Ki = 2.24 μM), respectively, for the [3H]N-methylscopolamine binding site on the M5 receptor. 56 was most selective in the series (11-fold selective for M5 over M1 mAChR, with little affinity for M2-M4); whereas, 28 had modest (6-fold) selectivity over M1. 56 was potent (IC50 = 0.45 nM; Imax = 50%) inhibiting oxotremorine-evoked striatal [3H]dopamine release. Simulation data indicated that 28 and 56 bind to the orthosteric binding site of M5 located near the extracellular end of TM3, TM5, TM6, and TM7.
Conclusions: Selective binding of 56 to M5 over M1-4 receptors, strongly suggest that 56 interacts with M5 receptors to inhibit muscarinic agonist-induced striatal DA release. Differences in binding affinities of 28 and 56 to M5 mAChR are explained by differential interactions with residues I193 and T194 from TM5 and by hydrogen bonding distances between the side chain of residue D110 and the cationic head groups of the compounds.
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INTEGRATED COGNITIVE ENHANCEMENT THERAPY AND PERSONAL THERAPY FOR SUBSTANCE MISUSING SCHIZOPHRENIA PATIENTS: INTERIM RESULTS ON THE FIRST 6 MONTHS OF TREATMENT.

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Aims: Impairments in cognitive and affective processing are core features of schizophrenia that are untreated by current pharmacotherapies, and contribute to high rates of substance use comorbidity in this population. This study sought to examine the initial effects of a novel, integrated cognitive and affective remediation intervention for the treatment of these deficits in substance misusing patients with schizophrenia.
Methods: A total of 32 patients with schizophrenia or schizoaffective disorder meeting moderate or greater criteria for cannabis or alcohol use addiction severity were randomized on a 2:1 basis to 18 months of integrated Cognitive Enhancement Therapy and Personal Therapy (CET/PT) treatment (n = 22) or usual care (n = 10). Patients were assessed on a battery of neurocognitive, emotion processing, and addiction measures prior to treatment and every 6 months for the duration of the study.
Results: Intent-to-treat analyses on the first 6 months of treatment with all 32 randomized patients showed large (d = 1.27) and significant (p = .046) differential improvements in overall neurocognitive function favoring CET/PT compared to usual care. Neurocognitive effects were particularly marked for improved reasoning and problem-solving abilities (p = .005). Early 6-month effects on emotion processing favoring CET/PT were also large (d = 1.14) and approached statistical significance (p = .059, one-tailed).
Conclusions: Integrated CET/PT is a feasible cognitive and affective remediation strategy for substance misusing schizophrenia patients. CET/PT demonstrates significant early benefits on cognition and emotion processing that are expected to translate into reduced substance use and improved functional outcomes.
Financial Support: National Institute on Drug Abuse (R21 DA-30763) and National Center for Research Resources (KL2 RR-24154) grants to Dr. Eack.

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DEVELOPMENT OF MIXED OPIOID AGONIST/ANTAGONISTS TO PREVENT REINSTATEMENT OF EXTINGUISHED COCAINE-SEEKING BEHAVIOR.

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Aims: KOR antagonists reduce stress- (but not drug-) induced reinstatement of extinguished cocaine-seeking behavior. In contrast, mixed-action KOR/MOR agonists acutely reduce cocaine self administration and drug- (but not stress-) induced reinstatement. We hypothesized that a mixed MOR/KOR agonist with KOR antagonist activity would prevent both stress and drug-induced reinstatement of extinguished cocaine-seeking behavior.
Methods: In mice, we tested two putative mixed opioid agonist/antagonists, (-)pentazocine and the novel cyclic tetrapeptide cyclo[Ala-D-Pro-Phe-D-Trp] (Cmpd 1), for opioid efficacy and selectivity in the 55oC warm-water tail-withdrawal assay, and then determined both compounds effects on the reinstatement of cocaine in a conditioned place preference (CPP) assay.
Results: (-)Pentazocine and Cmpd 1 demonstrated equivalent efficacy in the tail-withdrawal assay with ED50 (and 95% CI) values of 2.51(1.66-4.27) and 3.03(2.16-4.58) nmol, i.c.v., respectively. However, whereas (-)pentazocine antinociception was mediated by all three opioid receptors, the antinociception of Cmpd 1 appeared to be primarily mediated by KOR, with a small contribution by MOR. Pretreatment (10 nmol i.c.v., -3 h) with Cmpd 1 selectively antagonized KOR, whereas (-)pentazocine primarily antagonized DOR. Surprisingly, while pretreatment (-3 h/d, i.c.v.) with either compound dose-dependently prevented a 2-day stress-induced reinstatement, acute administration of Cmpd 1 but not (-)pentazocine blocked cocaine-induced reinstatement.
Conclusions: Overall, these data suggest that with its distinct activity profile, compound 1 is a promising lead compound for potential development, particularly as a therapeutic to prevent relapse to drug seeking behavior in abstinent subjects.
Financial Support: Funding provided by NIDA (DA023924 and DA032928) and the State of Florida, Executive Office of the Governor's Office of Tourism, Trade, and Economic Development.

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HIV TESTING AND SEXUAL RISK REDUCTION COUNSELING IN OFFICE-BASED BUPRENORPHINE/NALOXONE TREATMENT.

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Aims: Sexual risk behaviors contribute to HIV transmission risk among opioid dependent individuals. We aimed to evaluate the feasibility and preliminary efficacy of HIV testing with sexual risk reduction counseling for opioid dependent patients initiating office-based buprenorphine/naloxone on decreasing sexual risk behaviors.
Methods: We conducted a 14-week randomized, controlled trial with 30 patients (original goal of 114) assigned to receive buprenorphine/naloxone and HIV testing with Brief Sexual Risk Management (BSRM– 2 sessions) or Enhanced Sexual Risk Management (ESRM- 4 sessions). We compared behaviors and health outcomes at baseline and during the 3-month follow-up.
Results: Similar proportions receiving BSRM and ESRM underwent HIV testing (93% vs. 80%, p=0.28) and completed counseling sessions (80% vs. 67%, p=0.40). As planned, BSRM sessions were shorter compared to ESRM sessions [15.4 minutes vs. 23.4 minutes], with comparable manual adherence (p=0.80). Outcomes did not vary by BSRM vs. ESRM. Among all subjects and compared to baseline, sexual risk behaviors decreased during the 3-month follow-up: proportion reporting sex with a primary partner, sex with a partner who had other partners, and sex after using opioids (all p values <0.001). The majority completed the trial (73%). Abstinence was similar in both groups based on the proportions of opioid-negative (54%) and cocaine-negative (63%) urines. Compared to baseline, health-related quality of life improved during the 3-month follow-up (mean 66 vs. 75, p=0.008).
Conclusions: While recruitment of opioid dependent patients with sexual risk behaviors is challenging, HIV testing with sexual risk reduction counseling in office-based buprenorphine practice is feasible.
Financial Support: Robert Wood Johnson Foundation Physician Faculty Scholars Program

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BIOCHEMICAL, HISTOPATHOLOGICAL AND BEHAVIORAL CHANGES AFTER SINGLE AND REPEATED INHALATION OF A LOCAL EGYPTIAN GLUE.

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Aims: To extend our research on the investigation of the biochemical, toxicological and behavioral effects of inhaling Kolla ; a local glue widely abused by street children in Egypt.
Methods: Brain levels of GABA, dopamine and 5 HT measured by spectrophotoflourometric methods. Liver and kidney functions tested using standard kits and spectrophotometric or spectrophotoflourometric methods. Brain histopathology according to Drury & Wallington (1980). Behavioral changes using "conditioned avoidance" and "Radial Arm Maize" tests. Two concentrations of glue (5000 & 10000 ppm) were tested after single or 10 day repeated daily inhalation using toluene as a standard reference inhalant .
Results: Single inhalation of Kolla caused decrease in GABA brain levels; less remarkable after repeated inhalation. An increase in brain 5-HT and dopamine levels was recorded after single or repeated inhalation of Kolla which significantly affected liver and kidney functions leading to increase in GPT, Alkalinephosphatase, GOT, Urea and Creatinine levels . Repeated Kolla or toluene Inhalation showed no obvious effect on reference or working memory; or on unconditioned or conditioned reflexes . Inhalation of high concentrations of Glue (10000 ppm) or toluene (56450 ppm) caused loss of both reflexes. Repeated inhalation of Kolla caused remarkable histopathological changes in the rat's brain.
Conclusions: Single inhalation of the local Egyptian glue "Kolla" leads to remarkable decrease in brain GABA levels; which is less remarkable after repeated inhalation. Kolla single and repeated inhalation increased both dopamine and 5HT brain levels. Single and repeated inhalation of Kolla produces remarkable increase in serum liver enzymes, urea and Creatinine. Inhalation of Kolla caused no obvious effect on reference or working memory. Kolla (5000 ppm) did not affect unconditioned or conditioned reflexes. In a concentration of 10000 ppm it caused loss of both reflexes. Repeated daily inhalation of Kolla displayed marked histopathological changes in brain tissues
Financial Support: None

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SUBSTANCE USE AND MOTIVATIONS FOR VIOLENCE: EVENT-LEVEL ANALYSES OF GENDER DIFFERENCES IN ANTECEDENTS TO DATING VS. PEER VIOLENCE.

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Aims: Violence has been linked to substance use and can lead to injuries, psychological distress, and death. The Emergency Department (ED) provides an opportunity for screening and interventions to prevent violence among youth. Additional data is needed regarding antecedents of dating violence (DV) versus peer violence (PV) to develop ED-based interventions.
Methods: Participants were 599 patients screening positive for past 6 month drug use in an urban ED (ages 14-24; 65% presenting for violent injury and an age/sex matched comparison group; 43% female; 58% African-American). Participants completed timeline follow-back aggression modules (past 90 days) at Baseline, 6-, and 12-months. Multi-level logistic regressions using event-level data, nested by individual and time, examined demographics, substance use and reasons for incidents of DV and PV.
Results: Females reported 522 incidents of DV victimization, 361 of DV aggression, 241 incidents of PV victimization and 214 of PV aggression. Males reported 58 incidents of DV victimization, 37 of DV aggression, 466 incidents of PV victimization and 414 of PV aggression. Regarding substance use before/during conflict incidents, alcohol only use was more likely for incidents of PV and illicit drug use was more likely to be involved in DV. For conflict reasons, "angry/bad mood" and "jealousy/rumors" for aggression and victimization (and "sex" for victimization) were more likely to be motivations for DV. "Personal belongings," "retaliation," "personal space" and "aid due to physical attack" were more likely to be reasons for PV (aggression and victimization). Post-hoc analyses examining gender interactions revealed differences in substance use and reasons for DV versus PV.
Conclusions: ED based DV interventions for urban adolescents and young adults need to be tailored for substance use (alcohol, cocaine, sedatives) and reasons for violence, by gender and depending on type of violence (DV vs. PV).
Financial Support: NIDA R01 024646; NIDA T32 DA007267

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IDENTIFICATION OF DATA GAPS THAT PRECLUDE EVIDENCE-BASED DRUG CONTROL POLICIES AIMED AT REDUCING OPIOID ANALGESIC ABUSE.

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Aims: Recent national epidemiologic surveys and analyses of unintentional fatalities involving drugs suggest that opioid-use disorders are endemic in the US. While there are ecological data regarding trends in drug use, misuse, and abuse, they do not provide a clear understanding of the populations that are contributing to the adverse outcomes measured. This effort aims to examine available death and abuse data to better understand what information exists on populations at-risk and to identify data gaps that, if addressed, could better inform policy-making and implementation.
Methods: A structured review was conducted of recent, public national data sources (such as NSDUH, DAWN, TEDS, and NVSS mortality statistics) and relevant literature to categorize available information in an effort to characterize the following subpopulations taking opioid analgesics: 1) adherent patients with legitimate medical need and a prescription, 2) non-adherent patients with legitimate medical need and a prescription (eg, more than prescribed, mixing with other drugs or ethanol), 3) persons without legitimate medical need and a prescription (eg, purporting to be a patient/doctor-shopping), and 4) persons using opioids without a prescription.
Results: A substantial body of information exists to identify inappropriate use of opioid analgesics and its attendant consequences; however, far less is available to assess the relationships among legitimate medical need, presence/absence of a prescription, and use patterns with the occurrence of desirable or undesirable outcomes. Current information suggests a substantial proportion of fatal opioid-related overdoses occur in those who abuse opioids, obtained with or without a prescription.
Conclusions: The gaps identified include lack of detail about opioid-involved fatalities, such as accurate classification of the role of contributing drugs, and how many adherent patients with legitimate need could be harmed by measures aimed at reduced availability of pharmaceutical opioids.
Financial Support: Full-time employees of Purdue Pharma L.P.

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TREATMENT OUTCOMES FOR MJ DEPENDENCE AMONG ADOLESCENTS ATTENDING AN URBAN INTENSIVE OUTPATIENT TREATMENT PROGRAM.

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Aims: This study describes the association between certain baseline characteristics – psychiatric status, juvenile justice involvement, gender, use of substances other than MJ, and prior treatment at a residential level of care – and outcomes over 12 weeks in youth with MJ dependence in a community intensive outpatient program.
Methods: Data was abstracted retrospectively from clinical charts of n= 67 patients with MJ dependence admitted between October 2010 and April 2011. Using logistical regression and independent sample t-Tests, indicators of retention (# of sessions and # of weeks attended) were compared with baseline variables.
Results: Patients characteristics included: 65.7% male, 80.6% African American, mean age 17.39 years (range 14-21). A significant portion of the sample reported criminal justice involvement (65.7%) and experience psychiatric comorbidity, with 67.1% reporting either past or current mental health problems (mental health therapy and/or psychiatric medications). Overall, 22.4% of the sampled adolescents completed the IOP program. Criminal justice involvement was associated with increased treatment retention (# of session attended (p= .10) and statistically associated with # of weeks attended (p=.05)). Furthermore, current or past psychiatric treatment was significantly associated with increased treatment retention (# of sessions attended (p= .05))
Conclusions: The findings from this study expand the literature on enhancing treatment retention for at-risk urban adolescents with multiple treatment needs. Interventions to increase adolescent retention in substance abuse treatment should be tailored to identify those most likely to drop out of treatment. Consistent with existing research, individuals with less severity of symptoms (no psychiatric history) and less involvement with the criminal justice system have been identified as individuals where retention rates could be problematic.
Financial Support: Mountain Manor Treatment Center

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PROGESTERONE TREATMENT FOR COCAINE-DEPENDENT WOMEN: A PILOT TREATMENT TRIAL.

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Aims: This study evaluated the efficacy of oral micronized progesterone (PROG) for reducing cocaine use in women.
Methods: A 10-week double-blind treatment trial compared PROG (up to 400 mg/day, b.i.d.) to placebo (PBO) in cocaine-dependent women who were cocaine abstinent before randomization. Voucher incentives for attendance were used to enhance retention. Primary outcome measures included time to relapse, days of consecutive cocaine abstinence and retention. Response to a laboratory stressor, the Trier Social Stress Test (TSST) and treatment outcome was also explored.
Results: Out of 227 women assessed, 25 women entered the trial, with 10 stratified to the PBO Group and 11 to the PROG Group. Thirteen women (62%) completed the entire 10-week trial. Five patients (2 in the PROG group and 3 in the PBO group) did not relapse, i.e., remained cocaine abstinent, during the trial. Two other women, one in each group, also did not relapse, but did not complete the trial. For the remaining women, the mean number of days to relapse was 2.0 for the PROG group and 2.3 for the PBO group ($p > 0.05$). The mean number of consecutive days of abstinence was 7.5 for the PROG group and 9.0 days for the PBO group ($p > 0.05$). Among the 14 women who completed the TSST before randomization, increases in heart rate ($r = -.33$), anxiety scores ($r = -.37$) and cocaine craving ($r = -.34$) in response to stress were negatively correlated with the percentage of cocaine negative urines.
Conclusions: PROG was well tolerated, but due to the small sample size it was not possible to adequately determine if PROG may be an effective treatment for cocaine-dependent women. Although cocaine-abstinence rates were low, they could be potentially improved using voucher incentives contingent on cocaine abstinence. Lastly, the preliminary findings showing that increased stress reactivity was related to low rates of cocaine abstinence suggest that stress-reduction techniques could improve treatment outcome.
Financial Support: NIDA grants RO1 DA022218 (SME), K24 DA029647 (FRL) and KO1 DA022282 (SCR). Medication was provided by the Women's International Pharmacy.

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EVIDENCE FROM A CANNABIS USE DISORDERS MULTIPLE CAUSES MODEL FOR THE CANNABIS-TOBACCO COMBINATION KNOWN AS 'BLUNTS'.

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Aims: Globally, cannabis often is combined with tobacco before smoking. In the US, a prevailing cannabis-tobacco combination involves 'blunts,' made by substituting cannabis in a hollowed out tobacco cigar. Cannabis users with a history of blunt smoking seem to be at excess risk for cannabis use disorders (CUD). The aim here is to test a hypothesis that the profile of CUD clinical features is determined, in part, by blunt smoking history among cannabis smokers.
Methods: Data are from the nationally representative 2004 US National Survey on Drug Use and Health (NSDUH), with 7054 recent cannabis smokers age 12+ years, all with past-year cannabis use (6+ times), and with valid CUD and lifetime blunt history assessment. Exploratory factor analysis probed CUD latent structure (e.g., 1 v 2 factor model fit). Then, via a multiple indicators, multiple causes model (MIMIC), the blunt smoking effect was estimated for each CUD clinical feature, holding constant CUD level.
Results: Roughly 3/4s of recent cannabis users had smoked blunts at least once. EFA supported a 1-factor solution, and MIMIC modeling disclosed that blunt smoking was independently associated with "tolerance on" and "spending a great deal of time getting/using" cannabis, with CUD level held contstant. Inverse blunt associations were found for "giving up important activities", "failure to fulfill roles", and "continued use despite social problems" under this model (slope estimates: 0.18, 0.41, -0.25, -0.33, and -0.33, respectively; all p-values<0.02).
Conclusions: We discovered that blunt smoking seems to influence CUD clinical features, over and above CUD level. Whether the observed differences indicate substantive differences in blunt effects and/or disclose measurement bias are open questions. Answers to these questions will be needed if we are to make progress in our understanding of the epidemiology of the cannabis-tobacco combination.
Financial Support: NIDA T32DA021129 (BJF); K05DA015799 (JCA).

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PERSONALITY CHARACTERISTICS OF YOUNG ADULT, NON-MEDICAL PRESCRIPTION OPIOID USERS IN CENTRAL OHIO.

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Aims: Research suggests that personality traits are correlated with health compromising behaviors, including illicit drug use. This study's aim was to examine the racial/ethnic and gender differences in common personality traits among young adults who use prescription opioids non-medically.
Methods: Respondent-driven sampling was employed to recruit 396 young adults, 18-23 years old, in the Columbus, Ohio, area for participation in a natural history study of non-medical prescription opioid users who were not DSM-IV opioid dependent. The baseline assessment collected data in a number of areas including personality characteristics. Extraversion, agreeableness, conscientiousness, neuroticism and openness were assessed with the 44-item Big Five Inventory (BFI) and sensation-seeking with the 8-item Brief Sensation Seeking Scale (BSSS). Both instruments use scores ranging from 1 to 5 to assess trait presence, with higher scores indicating higher levels of a trait. Mean BFI and BSSS scores for non-white men, non-white women, white men, and white women were compared using ANOVA with post hoc pairwise comparisons using Tukey's HSD test.
Results: White women had a significantly higher mean extraversion score compared to non-white men (3.74 vs. 3.46, $p=0.039$), and a significantly higher mean neuroticism score compared to both white men (2.87 vs. 2.50, $p=0.015$) and non-white men (vs. 2.43, $p=0.003$). White men had a significantly lower mean conscientiousness score compared to both non-white men (3.66 vs. 3.98, $p\leq0.001$) and non-white women (vs. 3.90, $p=0.017$), and a significantly higher mean sensation-seeking score compared to white women (3.91 vs. 3.56, $p=0.018$), non-white men (vs. 3.31, $p\leq0.001$), and non-white women (vs. 3.02, $p\leq0.001$).
Conclusions: The results demonstrate an aspect of the heterogeneity of young adult prescription opioid users that was previously unknown. The findings can help inform the development of relevant prevention messages and intervention strategies.
Financial Support: NIDA grant R01DA23577 (R.G. Carlson, PI).

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DOES CUE TYPE MATTER FOR CRAVING? COMPARISON OF SUBSTANCE-SPECIFIC AND PERSON-SPECIFIC CUES USING MOBILE TECHNOLOGIES.

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Aims: Different individuals are exposed to the same paraphernalia for a given substance, but each individual has unique patterns and contexts of use. Our objective was to compare the influence of substance- and person-specific cues in the prediction of craving intensity and substance use.
Methods: 132 outpatients were recruited and completed 2 weeks of monitoring of daily life experiences using Ecological Momentary Assessment (EMA). The main substance of dependence was alcohol (n=39), opiates (n=32), tobacco (n=32), or cannabis (n=29). Patients described in real-time their exposure to substance-specific and person-specific cues. Data were analyzed using hierarchical linear models (HLM) to examine the influence of both types of cues on craving intensity.
Results: Craving intensity was strongly associated with number of concurrently-assessed substance-specific cues ($\gamma = 0.243$, $p<0.001$), and person-specific cues ($\gamma = 0.392$, $p<0.001$). Cross-sectional associations did not vary significantly by sex, and they remained significant when adjusted for type of substance. The association of alcohol cues with alcohol craving was significantly stronger than for tobacco or for opiates. Prospective analyses revealed that the number of substance-specific cues was not associated with craving intensity at the subsequent assessment 3 hours later ($\gamma = 0.044$, $p>0.05$), while person-specific cues strongly predicted craving intensity over this same time period ($\gamma = 0.126$, $p=0.004$). This prospective association did not differ by sex or type of substance.
Conclusions: This study provides highly novel information concerning the important role played by person-specific cues in determining craving intensity and the risk of substance use. Assessment of the practices that are unique to individuals may be more relevant to preventing relapse than commonly-examined cues shared across individuals for a given substance.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008, CNRS ATIP

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FEASIBILITY OF ADOLESCENT COMMUNITY REINFORCEMENT APPROACH AND CONTINGENCY MANAGEMENT IN A SPANISH CONTEXT.

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Aims: Among Spanish adolescents, 17% report cannabis use in the previous month (ESTUDES 2010). However, no Evidence-based treatment for Cannabis Use Disorders has been implemented in our country. The aim of this study was to assess the feasibility of a pilot implementation of the Adolescent Community Reinforcement Approach (ACRA) and Contingency Management (CM) in the Spanish Publich Health System.
Methods: The manual of ACRA (Godley et al. 2001) was translated into Spanish, and a schedule for CM was designed to reinforce abstinence. An experimental design with two groups (ACRA vs. ACRA+CM) was implemented in two outpatient facilities of the Spanish Public Health System: Proyecto Hombre Asturias (Oviedo) and MadridSalud (Madrid).
Results: Treatment demand was lower than expected: 92 eligible adolescents. Only 26 participants were allocated, due to exclusion criteria: most of them presented with mental health issues, lack of family support or other primary drugs of abuse. Most participants were male (91.7%) and mean age was 16.50 (SD = 1.18). Cannabis-related problems (CPQ-A), depressive (BDI-II) and internalizing symptomatology (CBCL) decreased significantly. Final retention was 81.3% in ACRA and 100% in ACRA+CM. Abstinence rates were 68.6% (ACRA) and 75.5% (ACRA+CM). No significant barriers prevented appropriate implementation of ACRA and CM.
Conclusions: Implementing selected EBTs in the Spanish Public Health System is feasible. Results indicated that positive outcomes can be obtained with regards to cannabis use and cannabis-related problems. However, future implementations could utilize group format, broader inclusion/exclusion criteria and some treatment adaptations to address barriers encountered.
Financial Support: The study was funded by the Spanish Ministry of Science and Innovation (MICINN-08-PSI2008-00309)

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FEASIBILITY OF A VISUAL PERFORMANCE FEEDBACK DURING JUDICIAL STATUS HEARINGS IN DRUG COURT.

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Aims: Visual aids have not been examined as a means to improve communication between drug court judges and offenders in the court room. A visual performance feedback tool was developed to enhance communication between them during judicial status hearings in drug court. The objective of this pilot study was to assess the clarity, acceptability and utility of the performance feedback procedure.
Methods: A pilot study was conducted during several status hearings of a drug court in Southern Delaware, USA. The sample included 16 consenting drug court clients, 16 consenting drug court observers and 11 drug court staff. Participants were asked to answer a 5-item questionnaire assessing the intelligibility, utility, acceptability and feasibility in drug court hearings of the performance feedback graph. The clients were also asked to interpret the behavior depicted in a sample graph. In parallel, a visual feedback procedure was developed and tested with five consenting clients during a live drug court session.
Results: Forty-two participants (98%) reported that the graphs were very easy/easy to understand. More than 75% of the drug court clients, observers and court staff considered that the graphs help the drug court clients to understand their progress. Sixteen clients (100%), 10 court staff (91%) and 15 observers (94%) reported that the graph added a value to the typical status hearings. Fifteen clients (94%) were able to correctly interpret the graph. The procedure was unanimously well-received by both drug court clients and staff.
Conclusions: A graphic performance feedback is feasible to implement in drug court. It appeared to be acceptable and understandable to drug court's clients and judges, indicating that it might be a useful tool to use in drug and other types of problem solving courts. An ongoing grant funded project is currently underway to examine the efficacy of the visual performance feedback in a larger sample.
Financial Support: NIDA Grant 5R01DA013096

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EFFECTS OF GENDER AND WEIGHT ON ERRORS OF OMISSION DURING AN INATTENTION TASK.

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Aims: Previous studies have established that obese adolescents possess a stronger tendency to behave more impulsively than do normal weight children (Braet, Claus, Verbeken, & Vlierberghe, 2007). Additionally, the claim that boys and girls possess different levels of impulsivity has also been substantiated by previous researchers (Moffit, Caspi, Rutter, & Silva, 2001).
For the current study, we sought to examine the relationship between gender, body weight, and impulsivity in adolescents measured by the number of errors of omission committed on a behavioral task of inattention. It was hypothesized that gender and body weight would have an interaction effect on impulsivity, such that obese males would be rated as the most impulsive group.
Methods: The study participants were 113 adolescents between the ages of 14 and 19. All participants completed a single laboratory session where height and weight were measured, and they performed a behavioral measure of impulsivity.
Results: A two-way ANOVA analysis revealed that the interaction between gender and body weight had an effect on impulsivity [$F(1, 112) = 6.47$, $p < .05$]. As we hypothesized, our findings indicate that males who were classified as overweight or obese scored higher on impulsivity (M = 94.12) than did obese females (M = 60.01), healthy weight males (M = 68.45), and healthy weight females (M = 65.31).
Conclusions: The findings indicate a gender difference in the effect of weight status on inattention and response rate, such that as males gain weight, their level of inattention also increases. This relationship appears more prominent in males and may present as a greater obstacle for treatment in this population. Therefore, it may be beneficial to include training programs to reduce impulsivity and inattention in overweight/obese males. These findings also indicate that this population may be more impulsive and consequently more susceptible to other risky behaviors, and therefore should be integrated into prevention and intervention efforts for risky behavior in adolescence.
Financial Support: The study was financially supported by Dr. Sherecce Fields, faculty start-up funds.

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A VIDEOGAME FOR SUBSTANCE USE PREVENTION AND HIV RISK REDUCTION IN YOUNG ADOLESCENTS.

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Aims: Substance use and associated HIV risk are prevalent among young teens. Given that the majority of young teens play videogames and there are emerging data that videogames can be effective as interventions for health conditions, we have developed an interactive videogame for risk reduction and HIV prevention in teens aged 11-14 years. The videogame PlayForward: Elm City Stories is an iPad application that represents the first game from a newly formed program. Play2Prevent™ (www.Play2Prevent.org) is a partnership between researchers, educators, videogame designers/developers, and community- based organizations to develop evidence-based targeted videogame interventions for risk reduction and prevention. Developing PlayForward involved formative work with focus groups and interviews with the target audience, an iterative process of feedback between the teen groups and the game developers, drafting of behavioral manuals based on well-established theoretical constructs such as prospect theory, and extensive play-testing. PlayForward, comprised of a series of stories that interlink with skill-based mini-games, is an interactive world in which the player, using an avatar "travels" through life, facing challenges and making decisions that bring risks and benefits. The content of the mini-games focuses on risk behaviors such as drug (prescription drugs, marijuana, inhalants) and alcohol use and sex. The player is able to see how their choices affect their lives and subsequently is able to go back in time to see how different actions might impact outcomes. By negotiating challenges in a repetitive and meaningful way, the player learns skills that potentially will translate to real life, equipping them to avoid situations that increase their risk for HIV.
Conclusions: This presentation will focus on the process of game and intervention development including multidisciplinary team building, focus groups, manual, story and videogame development, and will include video and screenshots from the game and describe a future randomized clinical trial.
Financial Support: Supported by R01HD062080

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COMMUNITY-BASED BUPRENORPHINE TREATMENT PROGRAM IN BALTIMORE CITY: REACHING AN UNDERSERVED POPULATION.

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Aims: Study aims were to: 1) report level of retention and completion of two novel community-based buprenorphine programs (CBBP) incorporated into recovery centers in Baltimore City, MD; and 2) assess whether retention rates differed from other bupenorphine programs (BPs). We hypothesized that CBBP, which targets underserved populations, would have comparable retention to that in a 2008 meta-analysis of BPs.
Methods: 196 individuals from two CBBP sites were included. CBBP "graduates" (n=94) were transitioned to ongoing care or transferred to higher level of care; non-graduates were non-adherent or lost to follow-up ("LTF", n=102). Individuals incarcerated during the CBBP were excluded (n=9). Descriptive statistics were used for demographic variables. Logistic regression was used to calculate the relative odds of treatment completion by treatment length. A two-sample t-test compared CBBP retention to BP retention.
Results: Participants were 58% male, 78% African-American, with a mean age of 45.8 years (SD=0.69). There were no differences in CBBP graduates and LTF demographics. With each additional week of CBBP participation, there was a significant 5% increase in odds of treatment completion (OR=1.05, 95% CI=1.02-1.08, p=0.002). CBBP retention was 0.48 (SD=0.50); this was not statistically different from the 0.52 (SD=0.07) retention reported in other BPs (t=1.75, df=635, p=0.08).
Conclusions: CBBP can be incorporated successfully in non-traditional community-based recovery centers with retention rates comparable to other BPs. This supports the hypothesis that integrating services into grassroots community sites trusted by the community residents is an effective treatment model. Future research should replicate CBBP in other settings to maximize access and reduce treatment inequity among vulnerable populations.
Financial Support: This study was supported by Behavioral Health Leadership Institute, Open Society Institute, and Abell Foundation.

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A PREDISPOSITION TOWARD INHERENT IMPULSIVITY IS ASSOCIATED WITH ELEVATED 5-HT2AR EXPRESSION.

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Aims: Poor inherent response inhibition, or "action without reflection," may set the stage for vulnerability to drug abuse and dependence. Serotonin (5-HT) systems play a nuanced role in impulsive action, perhaps mediated by forebrain 5-HT receptors. Selective 5-HT2A receptor (5-HT2AR) antagonists (e.g., M100907) reduce impulsive action with notable efficacy, suggesting that tonic 5-HT2AR signaling supports impulsive behavior. We sought to test the hypothesis that the inherent predisposition to impulsive action is associated with elevated forebrain 5-HT2AR expression and function.
Methods: These studies employed the one-choice serial reaction time (1-CSRT) task to identify high (HI) and low (LI) impulsive outbred rats. Rats were trained to nose-poke to receive a food reinforcer on a 5-sec inter-trial interval (ITI) schedule; responses during the ITI (premature responses) resulted in further delays of reward presentation. The upper 25% and lower 25% of animals were identified as HI or LI rats, respectively. Rats were sacrificed and the medial prefrontal cortex (mPFC) was harvested, and crude synaptosomal protein extracted for western blot analysis. In a separate set of animals, the ability of M100907 (0.003, 0.01, 0.03, 0.1 mg/kg, i.p.) to suppress premature responses was evaluated in HI and LI rats.
Results: HI rats displayed higher 5-HT2AR expression in crude synaptosomal fractions of the mPFC relative to LI rats ($p<0.05$, Student's t-test). Higher doses of M100907 (0.03, 0.1 mg/kg) suppressed premature responses in all rats, but lower doses (0.003, 0.01 mg/kg) suppressed premature responses selectively in HI, but not, LI rats ($p<0.05$, Dunnett's test).
Conclusions: These data demonstrate that high impulsive action is associated with elevated expression and enhanced function of the 5-HT2AR, suggesting that differential 5-HT2AR function in the mPFC may in part drive high and low impulsive action.
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STATISTICAL MODELS, MEASUREMENT AND NICOTINE DEPENDENCE THEORY.

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Aims: Use of complex multivariate statistical models is becoming common. Often these analyses use items and data that were not designed with a particular multivariate model in mind. For example, items may have been developed for surveillance or with a factor analytic model in mind but then used in cluster analysis. A common assumption is that these multivariate models pull out the important information in the data. This work examines this assumption. Nicotine dependence has been treated both continuously and categorically in the literature. However this choice is either assumed or an empirical attempt to decide is made. This research compares two simple and very similar latent variable models: the latent class and latent profile models. The scale of the data differs between these models, but the analytic goals are identical.
Methods: The Nicotine Dependence Syndrome Scale, administered as part of the 2004 National Survey of Drug Use and Health, is analyzed with both models. Raw data were recoded to sub-scale scores and binary indicators. To reduce heterogeneity, the sample was limited to white adults who reported daily smoking in the past 30 days (N=5,926).
Results: One expects data features driving the results to be strong. Arguably, the information in the positive/negative valence of the ordinal items should largely be captured in the binary data. However, starkly different results emerged, telling quite different substantive stories. In fact, psychometrically the importance of the subscales differed sharply between the analyses. In the latent class analysis, the subscales for drive/craving and tolerance are among the most important, whereas for latent profile analysis, the smoking priority sub-scale dominates.
Conclusions: Causes, implications, and recommendations are considered. Theory development hinges upon an evolving body of research. If results are conditional upon data features that should be ignorable or if salient data features vary by item scale, the value of these models to subsequent theory development is reduced.
Financial Support: This work was supported by National Institutes of Health grant R37DA18673 and a grant from the American Legacy Foundation.

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DIFFERENCES BY GENDER IDENTITY FOR INDIVIDUALS IN SUBSTANCE ABUSE TREATMENT.

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Aims: This study identified the characteristics and needs of transgender persons entering substance abuse treatment, a topic seldom addressed in the existing literature.
Methods: Substance use, psychosocial, health risk, medical, and mental health variables were examined in a database that documented individuals entering substance abuse treatment within San Francisco, CA between July 2007 and June 2009. Transgender (n=199) and non-transgender (n=13240) individuals were compared using logistic and linear regression.
Results: Transgender clients had unique patterns of substance use when compared to non-transgender clients, with higher rates of primary methamphetamine use (OR=2.01, 95% CI= 1.41-2.87) and higher rates of needle use (OR=1.44, 95% CI=1.05-1.98). Transgender clients were more likely to have physical health problems (OR=1.66, 95% CI=1.23-2.23), lifetime mental illness diagnoses (OR=2.75, 95% CI=2.04-3.69), be taking psychiatric medications (OR=2.58, 95% CI=1.92-3.47), have recent family conflict (OR=1.96, 95% CI=1.34-2.87), and recent alcohol use (B=1.24, p=.023). Transgender clients were also were less likely to be involved with the legal system (OR=.70, 95% CI=.51-.95), more likely to be in recovery oriented activities (OR=1.39, 95% CI=1.02-1.91), more likely to have been tested for HIV/AIDS (OR=2.50, 95% CI=1.66-3.77), and had lower rates of recent use of their primary substance (B=-2.65, p=.002). There were no detectable differences in recent work experience, arrests, ER visits, hospitalizations, mental health emergencies, hepatitis C/STD diagnoses, severity of substance use diagnoses, nor age first used primary substance.
Conclusions: Transgender individuals have unique needs in substance abuse treatment programs, including access to mental and physical health services. Transgender individuals may also bring inherent strengths, such as recovery involvement, to treatment.
Financial Support: National Institute on Drug Abuse: T32DA007250, P50DA09253, and U10DA015815.

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CONTINGENCY MANAGEMENT VOUCHER SPENDING AS AN INDICATOR OF DELAYED GRATIFICATION.

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Aims: This secondary analysis assessed the association between ongoing drug use and delays in earned CM voucher spending. It was hypothesized that drug use would be negatively associated with delays in voucher spending.
Methods: 131 homeless, substance-dependent (current methamphetamine dependence=63.4%) MSM enrolled in a voucher-based CM intervention. Participants were randomized into either a CM-Full or CM-Lite condition. All subjects earned vouchers for attendance/participation, while participants in the CM-Full condition also received vouchers for substance abstinence and prosocial behaviors. Longitudinal multivariate negative binomial regression analysis estimated associations between incidences of delayed spending and ongoing drug use, controlling for sociodemographics, condition assignment, total number of visits attended, and total number of vouchers earned.
Results: Participants were racially diverse (53.4% White) and averaged 36.4 years of age (SD=8.7). Seven participants did not earn/spend vouchers, making the final analytical sample n=124. Instances of delayed voucher spending were common (N=2777; avg. delay=13.2 days; SD=34.0). Participants delayed voucher spending for shorter intervals when testing positive for recent cocaine (IRR=0.77; 95% CI=0.68–0.88), methamphetamine (IRR=0.66; 95% CI=0.53–0.83), marijuana (IRR=0.75; 95% CI=0.66–0.85), or opiate (IRR=0.58; 95% CI=0.40–0.83) use.
Conclusions: Participants testing positive for recent drug use were less likely to delay voucher spending than those who were abstinent. Drug use has previously been associated with preference for immediate, rather than delayed gratification. Initial evidence suggests CM spending shares this association, and may be a valid indicator of the tendency to delay gratification. Thus, standard CM redemption logs may act as cost-effective and unobtrusive tools for measuring psychological functioning among participants enrolled in a CM intervention.
Financial Support: This study is supported by NIDA grant # R01 DA015990.

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PATIENT MOTIVATION AND 12-MONTH TREATMENT OUTCOME IN ALCOHOL USE DISORDER OUTPATIENTS IN FRANCE.

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Aims: Motivation for treatment was shown to be linked with treatment outcome, notably retention. The aim of this study was to identify baseline characteristics associated with 3, 6 and 12-month alcohol abstinence.
Methods: Consecutive patients from 8 nationwide alcohol addiction treatment outpatient clinics in France were asked to participate in the study. After informed consent, participants completed a baseline-structured-interview that included the Addiction Severity Index (ASI), the Mini International Neuropsychiatric Interview, and the SOCRATES a self-questionnaire to assess motivation. The ASI and the SOCRATES were repeated at 3, 6 and 12-month follow-ups. These data were examined as potential predictors of alcohol abstinence at 3, 6, and 12-month using multivariate regression models.
Results: 100 patients were included (74% males, 47.9 y.o.). The multivariate regression showed that a moderate to high Recognition score on the SOCRATES at baseline was linked to alcohol abstinence at 3 months (OR= 3.32, CI95%= 1.07 – 10.94). To be older (48+ y.o.) (OR= 4.78, CI95%= 1.42 – 18.65) and to present a high Ambivalence score on the SOCRATES at baseline (OR= 2.03, CI95%= 1.11 – 4.03) were linked to alcohol abstinence at 6 months. To have received previous treatments for alcohol (OR= 10.79, CI95%= 1.76 – 211.58) and to exhibit a high Recognition score on the SOCRATES at baseline (OR= 6.04, CI95%= 1.65 – 25.14) were linked to alcohol abstinence at 12 months. Overall, severity of baseline alcohol addiction and psychiatric comorbidities were not linked with alcohol abstinence at any follow-up.
Conclusions: In this sample, patient baseline motivation assessed by the SOCRATES was a better predictor of alcohol abstinence at follow-up than were psychiatric comorbidities and severity of alcohol addiction.
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EVALUATION OF PERCEIVED LACK OF CONTROL AS A MODERATOR OF THE RELATIONSHIP BETWEEN LESBIAN, GAY, AND BISEXUAL IDENTITIES AND ALCOHOL, TOBACCO, AND OTHER DRUG ABUSE AND DEPENDENCE.

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Aims: Perceived lack of control (PLC) has been associated with substance use and the experience of stress. The prevalence of substance use and stressful life events is high among lesbian, gay, and bisexual people relative to heterosexuals. This cross-sectional study aimed to determine the prevalence of PLC among sexual minorities relative to heterosexuals and to evaluate PLC as a moderator of the relationship between sexual identity and substance abuse and dependence.
Methods: A sample of 1,680 heterosexual and 577 sexual minority adults were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions, Wave 2 (2004-2005). PLC prevalence differences by sexual identity were determined and bivariate logistic regression models were estimated to evaluate the independent association of PLC with past-year alcohol, tobacco, marijuana and other drug (opioids, amphetamines, or cocaine) abuse or dependence. Logistic regression models were estimated to test the interaction between PLC and sexual identity.
Results: The prevalence of self-reported PLC was 27% among heterosexuals, 33% among gay and lesbian subjects, and 42% among bisexuals. PLC was significantly associated with past-year abuse or dependence of alcohol (OR 1.39), tobacco (OR 1.74), marijuana (OR 4.13), and other drugs (OR 2.72). In logistic regression analyses, the term for the interaction between sexual identity and PLC was marginally significant for past-year alcohol abuse or dependence [OR 1.40 (0.95-2.05), p=0.087] but not significant in the tobacco, marijuana, or other drug models.
Conclusions: This study confirms that the prevalence of PLC is elevated among sexual minorities relative to heterosexuals. While PLC does not appear to significantly moderate the association between sexual identity and past year alcohol, tobacco, marijuana or other drug abuse or dependence, future research should examine the possible association of PLC with alcohol, tobacco, and other substance abuse treatment seeking and effectiveness among sexual minorities.
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IMPACT OF A COMPLETE SMOKING BAN IN A DETOXIFICATION UNIT: 6-MONTHS EVALUATION STUDY.

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Aims: To evaluate the impact at 6 months of discharge, of the implementation of a complete smoking ban in a Detoxification Unit (DU).
Methods: Prospective study. All admitted patients between January and June 2011 at the DU of Hospital del Mar (Barcelona, Spain) were included. Sociodemographic, clinical data were recorded. Also, severity of nicotine addiction with Fagerström test and the use of Nicotine Replacement Therapy (NRT) required. Six months after hospital discharge, patients were contacted by telephone to assess the use of tobacco, and the Fagerström and Richmond (abstinence motivation) tests.
Results: The final sample consisted in 62 admissions (79% males; 45±10 years). The main drugs of admission were alcohol (54,8%), cocaine (16,1%), heroin (16,1%). The 94% of patients were nicotine dependent and the 87% required NRT during the detoxification (patches and gums the 91%). Treated patients smoked a mean of 23±11 cigarettes/day, Fagerström test at admission: 7±3 (severe dependence).
After 6 months, 18 (33%) were contacted. There were no differences between localized and non-localized patients. Fagerström at follow-up was 5±2 (moderate dependence), Richmond 5±3 (moderate motivation towards abstinence). Three patients remained tobacco abstinent after discharge during 2, 90 and 120 days respectively.
Conclusions: The majority of patients that are admitted in a DU required NRT, mostly combined. After discharge, without treatment for tobacco dependence, only 2 patients remained more than 90 abstinent. However, the severity of addiction decreased at follow-up and patients presented a moderate motivation towards a new quit trial. These results suggest the importance to offer nicotine dependence treatment after a detoxification discharge.
Financial Support: Support was received by Xarxa d'Hospitals Sense Fum (Spain).

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MORE "BATH SALTS": DISCRIMINATIVE AND LOCOMOTOR EFFECTS OF SYNTHETIC CATHINONES.

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Aims: Synthetic cathinones continue to be sold as "legal" alternatives to methamphetamine or cocaine. As these marginally legal compounds become controlled, suppliers move to other, unregulated compounds. The purpose of these experiments was to determine whether several uncontrolled cathinone compounds, which are currently abused on the street, stimulate motor activity and have similar discriminative stimulus effects with cocaine and/or methamphetamine.
Methods: Methcathinone, 4'-methyl-α-pyrrolidinopropiophenone (4-MePPP), pentylone, 5,6-methylenedioxy-2-aminoindane (MDAI) and 4-methylethcathinone (4-MEC) were tested for locomotor stimulant effects in mice and subsequently for substitution in rats trained to discriminate cocaine (10 mg/kg, i.p.) or methamphetamine (1 mg/kg, i.p.) from saline.
Results: Methcathinone and pentylone produced locomotor stimulant effects with efficacy ranging from 95% to 117% of cocaine or methamphetamine, which lasted up to 3 hours. In addition, pentylone produced seizures and lethality at 100 mg/kg. 4-MePPP and 4-MEC produced locomotor stimulant effects with efficacy ranging from 55% to 77% of cocaine or methamphetamine, which lasted up to 2 hours. MDAI depressed locomotor activity from 10 to 60 min. Methcathinone, 4-MePPP, pentylone and 4-MEC each produced discriminative stimulus effects similar to those of cocaine and methamphetamine. MDAI produced cocaine-like responding, but produced no methamphetamine-like responding. MDAI produced tremors at 10 mg/kg.
Conclusions: Methcathinone, 4-MePPP, pentylone and 4-MEC each produced discriminative stimulus effects similar to those of cocaine and methamphetamine, which suggests that these compounds are likely to have similar abuse liability. MDAI depressed locomotor and produced only some cocaine-like responding, so may be less attractive on the street. Both MDAI and pentylone produced dangerous adverse effects, which may warrant control of those compounds.
Financial Support: Supported by NIH N01DA-7-8872.

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SEX DIFFERENCES IN FUNCTIONAL CONNECTIVITY DURING SMOKING CUE EXPOSURE.

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Aims: Sex differences exist for the reinforcing and rewarding effects of nicotine with recent research suggesting sex-specific differences in neural responses to smoking cues. One factor that may contribute to differential responses to nicotine and nicotine-related factors is functional connectivity during smoking cue exposure. Based on our previous findings indicating that males exhibit greater hippocampal/amygdalar activation to smoking cues, we examined sex differences in functional connectivity with the hippocampal/amygdala region during smoking cue exposure.
Methods: Nicotine-dependent 'sated' smokers (N=51, 20 females) participated in a pseudo-continuous arterial spin labeling (pCASL) perfusion functional magnetic resonance imaging (fMRI) smoking cue reactivity experiment. Smoking cue fMRI data were preprocessed and analyzed in SPM8 using a seed-based correlation analysis with the bilateral hippocampal/amygdala region identified in our first study as seed regions of interest ($P < .01$ and clusters > 50 contiguous voxels).
Results: In females as compared with males, dynamic cerebral blood flow (CBF) within the hippocampal/amygdalar region demonstrated increased correlation with CBF variations in the bilateral medial frontal gyrus (Brodmann's Area 10) (females: left r = 0.83, right r = 0.72; males: left r =0.46, right r = 0.25).
Conclusions: Enhanced connectivity in females in these regions involved in memory and attention may be a mechanism underlying greater cue vulnerabilities. Studies are ongoing to examine whether increased connectivity in this circuit predicts relapse.
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METHAMPHETAMINE DEPENDENCE AND BRAIN ACTIVATION DURING RISKY DECISION-MAKING.

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Aims: Methamphetamine users exhibit greater impulsivity and impaired learning of stimulus-reward associations than healthy people who do not use the drug, but it is unclear how these differences may relate to decision-making. This study, therefore, aimed to compare the effects of recent experience on neural activity associated with decision-making in MA-dependent (MA, n=17) and healthy control (HC, n=14) research participants.
Methods: The participants underwent functional MRI while performing the Balloon Analogue Risk Task (BART), which presents successive choices either to pump a virtual balloon to increase potential monetary reward with increasing risk of explosion and loss, or to cash out to collect a reward, avoiding risk and loss. Successful trials end in cashing out, and unsuccessful ones end with the accumulated reward being lost when the balloon explodes.
Results: The groups exhibited similar risk-taking behavior, as indexed by the number of pumps made in trials after a loss, but they differed in regional neural activity. HC participants showed greater activation than MA participants in the ACC, striatum, parietal and prefrontal cortices while deciding to cash out after an unsuccessful trial.
Conclusions: The regions affected have been implicated in probability judgments, feedback processing, and stimulus-reward associations which are areas stimulant users have shown differences in from healthy people. A better understanding of differences in brain function associated with MA dependence, including activity related to decision-making, may be helpful in the design of behavioral therapies for this disorder.
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THE KAPPA AGONIST, SALVINORIN A, PUNISHES REMIFENTANIL AND COCAINE SELF-ADMINISTRATION IN MONKEYS.

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Aims: The study of drugs as punishers may be useful in the development of abuse-deterrent formulations for prescription medications. Kappa agonists, which have received much experimental attention as therapeutics for drug abuse, are reportedly dysphoric in humans and appear to be aversive in animals. The aim of the current study was to determine if a kappa agonist could punish self-administration of two drug reinforcers from different classes: the mu opioid, remifentanil, and the psychostimulant, cocaine.
Methods: Using a two-lever operant procedure, 4 monkeys were allowed to choose between equal doses of an intravenous drug reinforcer when the options were the drug alone or the drug mixed with a range of doses of the kappa agonist, salvinorin A (SVA). In separate conditions, the drug reinforcers were 0.1 μg/kg remifentanil (n=2) or 100 μg/kg cocaine (n=2). Daily sessions consisted of 2 forced-choice trials on each lever followed by 10 free-choice trials; trials were separated by a 10-min timeout.
Results: In the absence of SVA, choice for the lever paired with the drug alone option was approximately 50% for both the remifentanil and cocaine conditions. However, adding SVA to the mixture option increased choice for the drug alone option in a manner directly related to SVA dose for both remifentanil and cocaine. At the highest dose of SVA tested (10 μg/kg), choice for the drug alone option was >80% in all monkeys for both drug conditions.
Conclusions: These data indicate that the kappa agonist, SVA, can punish self-administration of remifentanil and cocaine in monkeys. These findings suggest a novel use for kappa agonists as therapeutics for drug abuse. Punishment of self-administration, as a mechanism, offers a specific utility for these compounds that likely capitalizes on their dysphoric effects.
Financial Support: This research was supported by R01-DA-019471 and R21-DA-0026832 from the National Institute on Drug Abuse.

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ORGANIZATIONAL FACTORS ASSOCIATED WITH HEPATITIS C TESTING IN OPIOID TREATMENT PROGRAMS: RESULTS FROM A NATIONAL STUDY.

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Aims: Hepatitis C Virus (HCV) is a major public health concern and particularly prevalent among persons who inject drugs. We examine rates of HCV testing in a national sample of opioid treatment programs (OTPs) and the extent to which organizational characteristics of OTPs are associated with the availability of HCV testing services.
Methods: We used multinomial logistic regression to examine organizational characteristics of OTPs associated with the availability of HCV testing services. Data were collected from a nationally representative sample of OTPs in 2005 (n=187) and 2011 (n=196). Program directors and clinical supervisors participated in a phone survey that collected data on the availability of HCV testing services as well as key organizational characteristics.
Results: The proportion of OTPs offering referrals only or offsite HCV testing increased from 20% in 2005 to 56% in 2005, with 10% of OTPs not offering any HCV testing in 2011 compared with 27% in 2005. However, on-site HCV testing declined significantly, from 53% in 2005 to 34% in 2011. The probability of onsite HCV testing was associated with hospital affiliation, greater staff-client ratio, and federal funding. While having some federal funding has a strong impact, and increases the probability of onsite testing compared with offsite and no HCV testing, the proportion of OTPs receiving any federal funding has declined considerably over time. Programs that use buprenorphine as the only method of treatment have increased probability of offsite testing.
Conclusions: Availability of on-site HCV testing services in OTPs is suboptimal. This presents a challenge to reducing the burden of hepatitis across the nation, particularly because clients referred offsite for health services have been shown to be less likely to follow-through on referrals. Investment and policy changes are needed to promote on-site hepatitis C testing in OTPs.
Financial Support: KL2 TR000081, R01DA030459

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GENDER DIFFERENCES IN STATE-DEPENDENT AFFECTIVE BRAIN FUNCTION AND MOTIVATIONS TO SMOKE.

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Aims: Smoking and negative affect are tightly intertwined—smokers report smoking in response to negative affect provoking stimuli, and negative affect precipitates relapse. Relatively little is known regarding gender difference in the effects of smoking withdrawal on neural processing of negative emotional stimuli. Moreover, relations between smoking motivations and neural reactivity to emotional cues remain unclear. The current study examined the role of gender in (a) neural reactivity to negative emotional cues under conditions of withdrawal vs. satiety, and (b) motivations to smoke.
Methods: BOLD-fMRI images were obtained while nicotine dependent female (n=8) and male (n=9) smokers viewed negative and neutral emotional images during two laboratory sessions: once following 24 hr. abstinence, once following smoking as usual. Baseline smoking motivations were assessed with the Wisconsin Inventory of Smoking Dependence Motives questionnaire.
Results: With regard to fMRI results, neural response to negative cues was modulated by a gender by smoking state interaction in right IFG—a region involved in inhibiting emotional interference; response was greater in females during abstinence but greater in males during satiety. Analysis of gender differences in smoking motivation revealed females were more motivated to smoke in response to cues, negative affect and to control weight whereas males were motivated by the sensory aspects of smoking. Finally, across all subjects, self-reported motivation to smoke to reduce negative affect predicted neural response to negative cues in medial frontal cortex (MFC)—a neural substrate of emotional arousal and self-referential processes.
Conclusions: The findings indicate that females and males process negative emotional cues differently as a function of smoking state that may explain, in part, gender differences in negative reinforcement of smoking behavior. Implications for understanding the relationship between gender and emotional function within the framework of smoking addiction will be discussed.
Financial Support: DA026536Z

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COMPARATIVE EFFECTS OF RACLOPRIDE IN TWO MODELS OF COCAINE-INDUCED REINSTATEMENT.

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Aims: To compare the effects of the D2 receptor antagonist raclopride in 2 different models of cocaine-induced reinstatement in the rat, the cocaine-induced (CIR) and cocaine + cue-induced (CCIR) reinstatement models.
Methods: All experiments were carried out in operant chambers equipped with two retractable levers, a cue light and a tone generator. Male Sprague Dawley rats were implanted with jugular catheters. Daily sessions of 2 hours duration were then conducted during which rats could receive infusions of cocaine (0.35 mg/kg/infusion) under FR1 schedule of lever pressing. When self-administration was acquired, rats were moved to extinction sessions in which active lever presses no longer produced drug infusion. After reaching the extinction criterion, rats were tested for reinstatement 30 minutes after being treated with either vehicle or raclopride (0.08 or 0.15 mg/kg s.c.).The CIR session was identical to the self-administration session except that no cocaine was delivered. For the CCIR session, rats received one non-contingent administration of cocaine (10 mg/kg i.p.) immediately prior to the session. The number of active lever presses during the reinstatement session, compared to extinction lever responding, was considered as a measure of reinstatement. The percentage of inhibition was analyzed by ANOVA with repeated measures.
Results: In vehicle-treated rats, a greater number of active lever presses were observed in the CCIR model. A consistent inhibitory profile on cocaine-seeking behavior was demonstrated for raclopride at the highest dose in both models whereas the suppressing effect at the lower dose was only observed in the CIR model. These data demonstrate that the CCIR model induces a higher level of drug-seeking than that produced in the CIR model which altered the sensitivity of raclopride.
Conclusions: The detection of efficacy with a test compound on preventing drug-seeking or relapse-like behavior may differ depending on the selected reinstatement model.
Financial Support: None

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ROLE OF DOPAMINE SYSTEM IN EXPRESSING BEHAVIORAL AND CYTOTOXICOLOGICAL PROPERTIES OF MDPV IN MICE.

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Aims: Products labeled as bath salts containing methylenedioxypyrovalerone (MDPV) are sold as recreational drugs. The aim of the present study was to investigate the behavioral and cytotoxicological properties of MDPV in mice.
Methods: In the present behavioral analysis study, we investigated the effect that MDPV has on locomotor activity and place conditioning in ICR mice and whether any of the associated effects discovered might be involved with the dopamine system. The cytotoxicological effects of MDPV were characterized in mouse striatal neurons of primary culture. At 24h, cytotoxicity was measured using a Cytotox-Glo cytotoxicity assay kit purchased from Promega.
Results: Administration of MDPV produced marked hyperlocomotion. In a place-conditioning study, MDPV produced a significant conditioned place preference. The stimulus and rewarding effects of MDPV were completely suppressed by dopamine D1 receptor antagonist SCH23390. MDPV produced a rapid increase in striatal dopamine release measured by in vivo microdialysis. Administration of MDPV in striatal primary culture caused cell death in a dose-dependent manner.
Conclusions: Our findings demonstrated that the dopamine D1 receptors might be involved in expressing MDPV-induced hyperlocomotion and the rewarding effect. The monoamine system, which is mainly the dopamine system, may play an important role in expressing MDPV-induced psychostimulant-like effects. These behavioral and neurochemical data indicate that MDPV might have a psychic dependence liability that is similar to that of psychostimulants. Furthermore, our data on striatal primary culture indicate that MDPV has strong neurotoxicity. These behavioral and neurochemical data indicate that MDPV might have strong adverse effects and a psychic dependence liability that is similar to that of psychostimulants.
Financial Support: This work 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.).

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DIFFERENCE IN TIME TO TREATMENT IN NEONATES EXPOSED TO BUPRENORPHINE OR METHADONE IN UTERO.

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Aims: Recommended standards of care call for treating opioid-dependent pregnant women with methadone and observing the exposed neonates for at least the first four days postnatal to see if treatment for neonatal abstinence syndrome (NAS) is needed. Data from a recent double-blind randomized clinical trial comparing methadone vs. buprenorphine for the treatment of opioid dependence during pregnancy suggest buprenorphine-exposed neonates had less severe NAS (less intense central nervous system signs, less medication needed to treat NAS) than methadone-exposed neonates, but that the NAS associated with buprenorphine may take longer to become clinically significant as measured by time to treatment initiation. The purpose of the present study was to see if time to treatment initiation differed in a non-blinded clinical sample of buprenorphine- vs. methadone-exposed neonates treated for NAS.
Methods: Medical records for 75 neonates exposed to either methadone (n = 28) or buprenorphine (n = 47) in-utero who required treatment for opioid withdrawal were examined. Time elapsed between birth and initiation of pharmacological treatment was calculated for each neonate and the mean time to treatment initiation compared between groups.
Results: Mean (hours:minutes, ± SE) time to treatment initiation differed significantly between groups (44:40 ± 6:28 for methadone vs. 72:40 ± 4:58 for buprenorphine, p=.001).
Conclusions: These findings confirm earlier results from a double-blind randomized clinical trial, adding generality to the observation that neonates prenatally exposed to methadone require treatment approximately a full day earlier than those exposed to buprenorphine. While the NAS associated with buprenorphine appears less severe in several respects, these data indicate that treatment providers should remain vigilant and also observe buprenorphine-exposed neonates for at least the first four days postnatal.
Financial Support: This study was supported by research grant R01 DA031928 from the National Institutes of Health, National Institute on Drug Abuse.

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INCORPORATING ADDICTION TREATMENT INTO MEDICAL HOMES FOR HOMELESS VETERANS: A 3-SITE COMPARISON.

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Aims: Veterans are overrepresented among homeless adults and have high rates of substance use disorders (SUD). Medical homes that offer integrated medical/mental healthcare are ideal settings to treat SUD in homeless adults. In 2012, the US Department of Veterans Affairs (VA) established medical homes for homeless Veterans at 32 sites. These Homeless Patient Aligned Care Teams (HPACTs) offer comprehensive primary care, SUD/mental health care and social services for homeless Veterans. We compare the early implementation processes and patient characteristics of 3 HPACTs in distinct US regions.
Methods: We compared the organizational processes of HPACTs at the VAs in Birmingham, Pittsburgh, and West Los Angeles (LA). We reviewed the charts of HPACT patients from 1/12-9/12 to obtain demographic, diagnostic and healthcare utilization data.
Results: Each HPACT reflected its location-specific context. Birmingham's HPACT is co-located with general primary care and offers specialized care for homeless Veterans, many of whom are identified by street outreach staff. Pittsburgh's HPACT is located within an existing PACT for Veterans with SUD and staffed by primary care and addiction medicine providers. LA's HPACT is a nighttime clinic co-located with the Emergency Room (ER) that targets homeless Veterans with high ER utilization. SUD prevalence differed markedly among sites. At Birmingham, Pittsburgh and LA, respectively, 63%/44%/35% of patients abused alcohol; 24%/16%/11% abused cannabis; 36%/23%/19% abused cocaine; and 9%/40%/6% abused opioids.
Conclusions: These 3 HPACTs incorporated SUD treatment into homeless healthcare in different ways. Enrolled Veterans at each site differ in SUD prevalence, reflecting local variations in SUD and historical entry criteria for local VA homeless programs. Further studies will explore if SUD outcomes improve with overall HPACT and addiction-specific engagement.
Financial Support: VA Office of Homeless Programs and Office of Primary Care

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A STANDARDIZED IN VITRO TEST BATTERY TO ASSESS TAMPER-RESISTANT PROPERTIES OF OPIOID FORMULATIONS.

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Aims: Among the various strategies to reduce prescription drug abuse introduction of tamper resistant formulations (TRFs) has proven to be an effective means to counteract abuse.
Therefore a standardized in vitro test battery to assess the tamper resistance of opioid formulations has been developed that addresses authorities demand for a comprehensive in vitro test battery that employs standardizable methodology and scientific rigor.
Methods: Grunenthal (GRT) has developed a four category test battery (INTAC® Test Battery) reflecting different classes of misusers/abusers and has allocated representative, standardized in vitro tamper test methods to those categories. Standard operating procedures (SOPs) have been created for the test battery.
Results: Examples for different misuser/abuser categories are given below:
In the the category "unintended misuse", a professional pill crusher, as used in nursing homes, was employed. After manipulation a TRF tablet only showed slight deformation but no pulverization. In vitro extended release properties of the manipulated TRF tablet were not affected (at 30 min; 120 min; 600 min 22; 51; 97 vs. 18; 44; 95 % of drug release were observed).
For the "recreational abuser" one test method employed a standardized hammering apparatus, simulating a stroke of a 500g hammer. Again the TRF tablet only showed slight deformation but no pulverization. In vitro extended release properties of the manipulated TRF tablet were not affected (at 30 min; 120 min; 600 min 20; 47; 96 vs. 18; 44; 95 % of drug release were observed).
To simulate tampering methods for the categories "experienced abuser" or "kitchen chemist", procedures for i.v. preparation and a battery of extraction media were standardized.
For the latter extraction ranged from 0 to 21 % and from 0 to 30 % for intact or manipulated tablets, respectively.
Conclusions: A standardized in vitro test battery was developed and the tamper resistant properties of an opioid TRF formulation were successfully demonstrated.
Financial Support: The study was supported by Grunenthal GmbH

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A BAYESIAN DOSE-FINDING TRIAL OF MODAFINIL FOR METHAMPHETAMINE DEPENDENCE.

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Aims: Modafinil blunts the effects of psychomotor stimulants in human laboratory studies. These trials do not indicate the optimal dose to test in outpatient clinical trials in which the main efficacy outcome is decreased use of stimulants. We conducted a Bayesian dose ranging trial of modafinil in methamphetamine (MA) dependence.
Methods: Eighteen MA dependent outpatients received modafinil (100, 400, or 600 mg per day) for four weeks. Subjects received weekly Motivational Interviewing and were assessed twice per week. The first subject was randomly assigned to 100 mg per day. Subsequent subjects were assigned to different dose groups using EffTox, a Bayesian dose finding computer program. Dose assignment was based on the results of prior subjects with respect to efficacy (defined as two or more MA-negative urine samples) and toxicity (defined as any adverse effect requiring discontinuation of modafinil).
Results: Two subjects were assigned to the 100 mg dose condition, 2 to the 400 mg condition, and 14 to the 600 mg condition. The next subject would have been assigned to the 600 mg condition.
Conclusions: Subsequent trials of modafinil for MA dependence should utilize a 600 mg dose of modafinil. Bayesian dose finding is a novel, rational method for selecting doses to be used in outpatient trials.
Financial Support: Supported by NIH R01 DA23567

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HIGH LEVEL EXPRESSION OF COCAINE HYDROLASE BASED ON MAMMALIAN CHOLINESTERASE BLOCKS COCAINE RESPONSES WITH NO SIGN OF TOXICITY.

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Aims: Cocaine hydrolase enzymes derived from bacterial and mammalian sources are being evaluated for treatment of cocaine addiction by reducing drug access to brain. We aimed to determine if massive over-expression of cocaine hydrolase (CocH) from mutated butyrylcholinesterase (BChE) interferes with cholinergic functions (locomotor activity), or cause toxicity in key organs To avoid complications from immune responses we produced a murine version, "mCocH", to test in mice (poster by Geng et al).
Methods: Mouse BChE cDNA with five mutations incorporated into helper-dependent adenovirus with ApoE promoter was given i.v. in a large dose of 2 x 1012 viral particles. Plasma cocaine hydrolase activity was monitored by radiometric assay. Plasma was also analyzed for toxicity as shown by sentinel enzymes: liver alanine amino transferase (ALT), and heart- and skeletal muscle-specific troponin-I. Muscle function (grip strength) was tested with a strain gauge. Spontaneous activity and locomotor responses to cocaine were evaluated in activity chambers.
Results: Mice given mCocH vector remained phenotypically normal despite a more than 1000-fold rise in plasma BChE. Spontaneous locomotor activity, gait, grip strength and grooming behavior were as in untreated control mice. There was no biochemical evidence of toxicity in muscle or heart as reflected in plasma troponin-I levels, or in liver as reflected in plasma ALT. But unlike controls, mice given HD-Ad vector showed a complete absence of hyper-locomotion or other external reaction after cocaine in i.p. doses of 40 mg/kg or 120 mg/kg (near lethal in controls).
Conclusions: Our findings show that mCocH at extremely high levels causes little direct physiological effect on mice but will block action of massive cocaine doses. This outcome justifies continued exploration of CocH gene transfer with regard to its potential for reducing risk of relapse into drug-seeking after a period of abstinence.
Financial Support: NIDA Avant-Garde Award DP1-DA31340 and R01-DA23979

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EXAMINING THE PSYCHOLOGICAL MECHANISMS OF PSILOCYBIN-ASSISTED SMOKING CESSATION TREATMENT: A PILOT STUDY.

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Aims: Anthropological evidence and early experimental studies suggest that structured administration of 5-HT2A agonist hallucinogens (e.g., LSD, psilocybin) may have potential in treating addictions, including alcoholism and opioid dependence. Psilocybin administration has been recently linked to persisting effects including personality change (i.e., increased NEO Openness), mood enhancement, and behavior change. The association between mood, personality, and addiction has been well documented, and suggests that psilocybin may be useful in the treatment of addiction. Although neurochemical mechanisms may be implicated, persisting psychological effects may also play a major role in modulating addictive behavior. The aim of this study is to assess the feasibility of psilocybin as an adjunct to addiction treatment, and to examine potential underlying psychological mechanisms.
Methods: We have developed a smoking cessation protocol integrating elements from Cognitive-Behavioral Therapy and mindfulness with 3 moderate to high dose sessions of psilocybin (20, 30, and 30 mg/70 kg). In order to examine psychological mechanisms related to psilocybin-assisted treatment, measures of self-efficacy for smoking abstinence, mindfulness, purpose in life, affect, perceived stress, withdrawal, and smoking urges were administered pre and post psilocybin sessions, and at 6 month follow up.
Results: Pilot results have been positive, with biologically verified abstinence (CO and cotinine) achieved by 100% of participants in the current sample of 5 volunteers at the 6 month follow up. Results generally showed increases in smoking abstinence self-efficacy, confidence, purpose in life, and improved concentration, as well as decreases in withdrawal related anxiety, craving, temptation, desire, and intention to smoke.
Conclusions: These findings are limited by the small participant sample; however this pilot study is ongoing and further volunteers are currently enrolled. Implications and future directions for research will be discussed.
Financial Support: Heffter Research Institute; NIDA T32DA07209

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DOPAMINE D3 RECEPTORS UNDERLIE COCAINE-INDUCED CONDITIONED PLACE PREFERENCE IN MICE.

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Aims: The dopamine D3 receptor (D3R) has received attention as a target for anti-addiction medication development, using selective D3R antagonists in animal models of addiction. The present work was undertaken to determine whether D3R gene deletion (KO) affects cocaine-induced conditioned place preference (CPP). Another aim was to study the effect of the novel D3R antagonist YQA14 on cocaine-induced CPP in wild-type (WT) mice.
Methods: Male WT and D3 KO mice and a standard mouse CPP apparatus were used. On days 1-3 mice had free access to both CPP chambers. On days 4-13 mice received saline or cocaine and confined to a treatment-specific CPP chamber. On day 14, mice were allowed free access to both chambers. Experiment 1 tested cocaine-induced CPP in WT mice. Experiment 2 compared cocaine-induced CPP between WT and D3 KO mice. Experiment 3 tested the effect of YQA14 on acquisition of cocaine-induced CPP. Experiment 4 tested the effect of YQA14 on expression of cocaine-induced CPP. Data were analyzed using paired t-tests or one-way analyses of variance.
Results: WT mice showed a dose-orderly cocaine-induced CPP. D3 KO mice showed an attenuated cocaine-induced CPP compared to WT mice. YQA14 pretreatment (10 days) inhibited acquisition of cocaine-induced CPP in WT, but not in D3 KO mice. Acute YQA14 pretreatment (20 mins before test) inhibited expression of cocaine-induced CPP in WT, but not in D3 KO mice.
Conclusions: Functional D3Rs are important for acquisition and expression of cocaine-induced CPP. The anti-addiction profile shown by YQA14 is extremely similar to that of SB277011A and NGB2904. The D3R remains an exceptionally attractive pharmacological target for the development of anti-addiction medications. YQA14 should be further studied to determine its anti-addiction potential.
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SCREENING FOR SUBSTANCE USE PROBLEMS IN PRIVATE U.S. HEALTH PLANS.

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Aims: Despite availability of validated screening instruments and national efforts to encourage screening there is still significant need for improved detection of substance use problems. Health plans can promote expanded screening by imposing requirements in primary care, aligning payment policies, or conducting screening independently.
Methods: Data are from a nationally representative, telephone survey of US private health plans in 2010 (89% response rate). For each of the three most commonly purchased insurance products, respondents reported on use of specific screening instruments (e.g., DAST) or general tools; screening, brief intervention and treatment (SBIRT) for alcohol problems; billing for screening; and plans' independent screening activities. Results are weighted to provide national estimates.
Results: In 2010, 18% of products required screening for alcohol and drug abuse problems in primary care using general instruments and 15% required specific screening instruments. Among the 96% of products that encouraged SBIRT, 99% did so through provision of guidelines, 41% through provider feedback, 51% by offering financial incentives, 3% by recognition programs, and 6% through training. Primary care providers (PCP) could bill for substance abuse screening and brief intervention in 72% of products. In terms of health plans' independent screening activities, 92% conducted screening by phone, mail, or web-based surveys. Positive screens triggered notification of the PCP for 25% of products and follow-up with the enrollee for all products.
Conclusions: Although screening is an effective way to improve the identification of substance use problems, most health plans do not require screening in primary care. However, they do use a range of approaches to promote screening, including payment, training and guidelines. Research is needed on the effectiveness of these approaches. This survey was focused on health plan activities, thus these results do not reveal the level of screening in primary care.
Financial Support: National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse

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OPEN-LABEL 24-MONTH STUDY OF INJECTABLE EXTENDED-RELEASE NALTREXONE (XR-NTX) IN HEALTHCARE PROFESSIONALS WITH OPIOID DEPENDENCE.

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Aims: This pilot study evaluated the long-term safety, tolerability and efficacy of injectable, once-monthly, intramuscular XR-NTX in opioid dependent healthcare professionals.
Methods: After detoxification, intramuscular XR-NTX was offered for up to 24 months.
Results: Of 49 patients screened, 38 (77.6%) began XR-NTX. The majority (N=31; 81.6%) were female nurses. Fifteen (39.5%) remained in treatment for 24 months. While receiving XR-NTX, four patients had opioid positive urine drug tests: 2 were in month 1; 3 patients discontinued and 1 patient continued in the study with negative opioids on all subsequent urine tests. There was a 37.8% reduction from baseline to month 24 in the mean opioid craving score. On the SF-36, (norm=50), mean SF-36 Physical Component Scores remained stable: BL=52.2, 24-mo=53.4; however, Mental Component Scores began ~1.5 standard deviations below normal, BL=36.3, and rose at 24 months to 47.6, for a mean change of 11.3 (>1 standard deviation). Mean Global Treatment Satisfaction Score was 93.2 (max=100) at 24 months. Common adverse events included nausea (42.1%), injection site pain (36.8%), anxiety (28.9%), and headache (26.3%); 18.4% discontinued due to adverse events and 18.4% were lost to follow-up. No patient experienced a drug-related serious adverse event and none died, overdosed or discontinued due to serious adverse events. Limitations include small sample size, open design and the unique population.
Conclusions: These results, in at-risk health professionals, indicate good long-term persistence on XR-NTX, high rates of opioid negative urines, reduction in opioid craving, improvement in mental health functional quality of life, and no new safety concerns.
Financial Support: Funded by Alkermes, Inc. Drs. Gastfriend, Memisoglu and Silverman are employees of Alkermes, Inc. Dr. Earley is a paid consultant to Alkermes. Injectable extended-release naltrexone (Vivitrol®) was developed with support from National Institute on Drug Abuse Grant R43DA013531 and National Institute on Alcohol Abuse and Alcoholism Grant N43AA001002.

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BEHAVIORAL EFFECTS OF SYNTHETIC CANNABINOIDS MARKETED AS "SPICE"

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Aims: A number of cannabinoid compounds are being sold as "legal" alternatives to marijuana in the form of incense. As these marginally legal compounds become controlled, suppliers move to other, unregulated compounds. The purpose of these experiments was to determine whether some common synthetic cannabinoids have discriminative stimulus effects similar to Δ9-tetrahydrocannabinol, which is thought to be the main active component in marijuana.
Methods: The compounds JWH-203, JWH-250, and AM2201 were tested for locomotor stimulant effects in mice and subsequently for substitution in rats trained to discriminate Δ9-tetrahydrocannabinol (3 mg/kg, i.p.).
Results: JWH-203, JWH-250, and AM2201 each decreased locomotor activity for up to 90 min. JWH-203, JWH-250, and AM2201 each fully substituted for the discriminative stimulus effects of Δ9-tetrahydrocannabinol at doses that did not alter rate of responding.
Conclusions: JWH-203, JWH-250, and AM2201 each decreased locomotor activity for up to 90 min. JWH-203, JWH-250, and AM2201 each fully substituted for the discriminative stimulus effects of Δ9-tetrahydrocannabinol at doses that did not alter rate of responding.
Financial Support: Supported by NIH N01DA-7-8872.

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TRAUMA EXPOSURE AND PTSD IS ASSOCIATED WITH ATTENUATION IN FRONTO-LIMBIC FUNCTIONAL CONNECTIVITY AMONG COCAINE USERS.

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Aims: Individuals with substance use disorders exhibit poorer treatment outcome, greater functional impairment and higher risk for relapse when presenting with comorbid trauma exposure or posttraumatic stress disorder (PTSD). These two comorbidities have, in several clinical populations, been linked to poor functional connectivity (FC) between the amygdala and medial prefrontal cortex (AMYG-mPFC) during tasks that probe emotional regulation. We hypothesized that this "biomarker" of emotional dysregulation might be detected even in the resting state, for cocaine-addicted individuals with co-morbid trauma and PTSD.
Methods: 36 stabilized detoxified cocaine patients were divided into three groups based on trauma status and PTSD diagnoses (NoTrauma, n=15; TRAUMA-NoPTSD, n=10; PTSD, n=11), using related questions from the Addiction Severity Index and the MINI psychiatric interview. Arterial spin labeled perfusion fMRI measured resting rCBF. Perfusion data were pre-processed with SPM8, using FC analyses with AMYG as the seed region.
Results: The NoTrauma group evidenced robust positive FC between AMYG-mPFC ($p<.001$(uncorr.), $t=11.90$), a pattern that progressively diminished for the TRAUMA group ($p<.001$(uncorr.), $t=6.03$) and was absent for the PTSD group.
Conclusions: As hypothesized, cocaine patients with TRAUMA and PTSD exhibit abnormal FC in regions responsible for regulation of affect and motivation—even in the resting state. Diminished AMYG-mPFC FC in the resting state may reflect an underlying dysfunction that manifests more fully during tasks that make demands on this connectivity (e.g., regulation of appetitive craving and/or aversive motivation). Our ongoing studies will test whether this biomarker of compromised fronto-limbic connectivity can predict clinical outcomes, including relapse.
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GENE TRANSFER OF ENGINEERED COCAINE HYDROLASE: LIFETIME EXPRESSION WITH NO IMMUNE RESPONSE.

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Aims: Recent animal studies show viral gene transfer of a cocaine hydrolase (CocH) based on mutated human butyrylcholinesterase lowers cocaine reward and impairs cocaine-primed reinstatement of drug seeking, but antibody response to foreign protein limits enzyme levels. Before CocH gene transfer is tested in cocaine users, to determine if mutation for fast cocaine hydrolysis stimulates immune reaction, we examined expression level and antibody responses in mice transduced with equivalent mutated mouse cholinesterase (mCocH).
Methods: mCocH cDNA with five mutations (A199S/S227A/S287G/A328W/Y332G) was incorporated into plasmid for HEK 293 cell culture and viral vectors for mouse injection. Enzyme was purified from culture supernates on procainamide-Sepharose. Molar levels were established by active site titration. Mouse tail-vein blood samples were drawn for radiometric assay of cocaine hydrolase and determination of anti-CocH IgG and IgM by solid phase precipitation.
Results: Substrate kinetics of mCocH showed 10-fold increased efficiency in cocaine hydrolysis (vs 1300-fold with same mutations in human CocH). Mice given 7 x 1010 viral particles (VP) of AAV vector showed a 10-fold rise in plasma CocH activity for 18 months or more, while 3 x 1011 VP generated a 30-fold rise. HD-Ad vector (2 x 1012 VP) was more effective, with a 300,000-fold rise of CocH activity and 500-fold increase in enzyme protein, for >6 mo at ~ 50% of peak. Circulating anti-CocH IgG or IgM antibodies were not detected. Hence the enzyme mutations were weakly antigenic. Other observations (poster by Gao et al) indicate that vector-delivered mCocH lacks toxicity across a range of systems and tissues.
Conclusions: Our findings show that mCocH at extremely high levels causes little direct physiological effect on mice but will block action of massive cocaine doses. This outcome justifies continued exploration of CocH gene transfer with regard to its potential for reducing risk of relapse into drug-seeking after a period of abstinence.
Financial Support: NIDA Avant-Garde Award DP1-DA31340 and R01-DA23979

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NICOTINE VAPOR INHALATION ESCALATES NICOTINE SELF-ADMINISTRATION.

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Aims: Humans escalate their cigarette smoking over time. This study addresses a major obstacle in the field of pre-clinical nicotine addiction research, which has been the inability to produce escalated nicotine self-administration in rats.
Methods: In Experiment 1, male Wistar rats were trained to respond for nicotine in 2-hr operant sessions, then exposed to chronic intermittent (12 hrs/day) nicotine vapor and repeatedly tested for nicotine self-administration at 8-12 hrs withdrawal. Rats were tested intermittently on days 1, 3 and 5 of the vapor exposure procedure, then tested on consecutive days 6-15 of nicotine vapor exposure. In Experiment 2, rats were exposed or not exposed to chronic intermittent nicotine vapor, then tested for spontaneous and precipitated somatic signs of nicotine withdrawal.
Results: Rats exhibited transient increases in operant nicotine responding during intermittent testing, regardless of vapor condition, and this responding returned to baseline levels upon resumption of consecutive-days testing (i.e., nicotine deprivation effect). Nicotine vapor-exposed rats then escalated nicotine self-administration relative to both their own baseline (~200% increase) and non-dependent controls (~3x higher). Eight hrs following removal from nicotine vapor, rats exhibited robust mecamylamine-precipitated somatic signs of withdrawal. There was a strong correlation between nicotine flow rate and air-nicotine concentration, and the air-nicotine concentrations used here resemble concentrations experienced by human smokers.
Conclusions: These results suggest that chronic intermittent nicotine vapor inhalation produces somatic and motivational signs of nicotine dependence, the latter of which is evidenced by escalation of nicotine self-administration.
Financial Support: This work was funded by AA018400 and LSUHSC SOM Faculty Start-Up Funds.

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ASSOCIATION OF COGNITIVE FUNCTIONING WITH TREATMENT OUTCOMES OF SUBSTANCE-DEPENDENT ADULTS WITH MAJOR DEPRESSION.

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Aims: Many evidence-based behavioral interventions for addictions, such as cognitive behavioral therapy (CBT) and motivational interviewing (MI), assume adequate cognitive functioning. Those with relatively lower cognitive ability may be particularly vulnerable to poorer treatment outcomes. Individuals with major depression suffer from cognitive symptoms; likewise, chronic substance use is associated with neurocognitive impairments. In a pilot randomized clinical trial (N=70), we evaluated: (1) changes in cognitive functioning from baseline to treatment-end; and (2) the effects of baseline cognitive functioning on outcomes of a 12-week continuing care intervention targeting depression and drug dependence.
Methods: Group CBT plus MI (CBT-MI) was compared to a control condition (dual recovery anonymous group: DRA) among depressed, substance dependent adults who were completing day hospital treatment for co-occurring disorders.
Results: A group-by-cognitive functioning interaction was observed, indicating that depressive symptom severity changed differentially over time as a function of overall cognitive ability and intervention condition, with CBT-MI participants with high cognitive ability reporting greater reductions in depression (Effect Size=0.95), relative to those with low cognitive ability. Likewise, a greater proportion of those in the CBT-MI condition evidenced stable or improving levels of cognitive ability from baseline to treatment end, relative to those in DRA, for whom declines in cognitive functioning were more frequently observed (Effect Size=0.28). Analyses of substance use outcomes in association with cognitive functioning and intervention condition are presently under way.
Conclusions: Among substance users with comorbid depression, some recovery in cognitive ability may occur in response to CBT- and MI-based interventions, and depression treatment response to CBT-MI may vary as a function of pre-treatment cognitive ability.
Financial Support: This research was supported by NIDA (K23 DA020085).

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NICOTINE, HPA AXIS HORMONES AND MOOD STATES IN WOMEN.

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Aims: To determine the acute effects of cigarette smoking on hypothalamic-pituitary-adrenal axis hormones and mood states in healthy nicotine dependent participants as a function of the menstrual cycle.
Methods: The acute effects of cigarette smoking on hypothalamic-pituitary-adrenal axis hormones and mood states were studied in 17 healthy nicotine dependent participants during the mid-follicular and mid-luteal phases of the menstrual cycle. Due to observation of a possible bimodal distribution of progesterone levels within the luteal phase group, we also performed a set of a posteriori analyses. Therefore, we divided the luteal group into a low progesterone group and a high progesterone group.
Results: Due to observation of a possible bimodal distribution of progesterone levels within the luteal phase group, we also performed a set of a posteriori analyses. Therefore, we divided the luteal group into a low progesterone group and a high progesterone group. These analyses revealed that the high progesterone group, compared with the follicular group, displayed lower increases in ratings of rush and high from baseline and less decrease from baseline in craving, that were statistically significant and represented large effects. Additionally, the high progesterone luteal group displayed a significantly lower mean peak DHEA than the follicular group.
Conclusions: These results are consistent with the possibility that progesterone modulates DHEA levels, which in turn has been implicated in drug addiction. Although much remains to be learned about the interactions between cigarette smoking, HPA axis and neuroactive gonadal steroid hormones, medications that mimic or attenuate the hormonal effects of cigarette smoking may be useful for treatment of this addictive disorder.
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MOTIVATIONAL INTERVIEWING COMBINED WITH CHESS IMPROVES WORKING MEMORY AND REDUCES IMPULSIVITY IN COCAINE DEPENDENCE: A PILOT INTERVENTION.

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Aims: Executive Functions (EF) deficits in Cocaine Dependence (CD) are associated to poor treatment outcome. Studies on EF rehabilitation in CD are scarce; besides, psychological interventions show modest effect sizes and pharmacological approaches have not proven their effectiveness. Our aim was to examine the effects of Motivational Chess (MC), a model integrating Motivational Interviewing and chess game on EF, especially working memory and planning.
Methods: 27 inpatients between 18-45 y.o. with crack cocaine or cocaine dependence were divided in two groups: MC (n = 14), and the Active Control (AC) group (n = 13), and assessed pre and post stimulation (during one month of abstinence monitored by urine toxicology) using neuropsychological tests and an impulsivity self-report scale. Statistical analyzes were performed using the SPSS version 14, and the ANOVA was used in the analysis of interaction among the assessments and the groups
Results: MC and AC were not statistically different in socio-demographic variables, IQ, neuropsychological tests and impulsivity scores at pre stimulation assessment. However, it was observed a group-by-time effect, the MC group showed a more significant improvement on working memory [$F(X,YY) = 4.375$, $p = 0.04$] and greater reduction on planning impulsivity [$F(X,YY) = 4.310$, $p = 0.04$].
Conclusions: Our results are promising due to the association of MC to EF enhancement and also to the feasibility of MC. The impact of MC in treatment retention and patients prognosis is an area to be investigated.
Financial Support: Brazilian National Counsel of Technological and Scientific Development (CNPq)

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PERCEPTIONS ABOUT RECOVERY NEEDS AND DRUG AVOIDANCE BEHAVIORS AMONG SUBSTANCE-ABUSING YOUTH.

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Aims: This study was conducted with youth in treatment to explore recovery-related needs and important drug avoidance behaviors after treatment.
Methods: A total of 14 focus groups were conducted with 118 substance-abusing youth in treatment (4 residential and 10 outpatient settings) throughout Los Angeles County, California between September and December 2010. Focus groups averaged 90-minutes and were transcribed for coding-theme generation.
Results: The average age was 17.4 (SD=2.9; range 12-24); 78.3% were male, 66.1% Latino; and most were in treatment for primary marijuana (40.9%) or methamphetamine (30.4%). Quantitative results identified the following factors youth rated as important to their recovery after treatment: lifestyle improvement activities (95.7%), changing personal drug behaviors (89.6%), drug environment/culture change activities (82.5%), with the least important being therapeutic activities (78.5%). Focus groups asked what youth think are important for recovery programs to address after treatment. Results revealed: (1) recovery promotion to developmentally appropriate activities (95%), (2) facilitating the use of coping skills to deal with stress (85%), (3) offering alternative recovery support options (not just abstinence only) (75%), and (4) continuing to provide substance use education (65%).
Conclusions: Findings highlight essential aspects of recovery in terms of need and drug-avoidance behaviors considered important to youth in treatment. Such information will help to better address clinical and recovery support models aimed at relapse prevention to ensure that the perceived problems of substance abusing youth are adequately met.
Financial Support: This study is supported by grant number K01 DA027754 from the National Institute on Drug Abuse (NIDA).

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HAZARDOUS DRINKING AND HIV RISK-RELATED BEHAVIOR AMONG MALE CLIENTS OF FEMALE SEX WORKERS IN TIJUANA, MEXICO.

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Aims: Describe patterns of alcohol use through a standardized scale, determine factors that are associated with hazardous alcohol use, and explore associations of hazardous alcohol use with HIV risk related behavior. We hypothesized that those clients who engaged in hazardous alcohol use would be more likely to report high-risk sexual behaviors with female sex workers after adjusting for sociodemographic variables, than those who did not engage in this behavior.
Methods: We recruited 400 male clients of female sex workers in Zona Norte, Tijuana, Mexico in 2008. Participants were interviewed and tested for HIV, syphilis, Chlamydia and gonorrhea. We characterized alcohol use thru Alcohol Use Disorder Identification Test (AUDIT). We describe AUDIT scores, patterns and frequency of drinking, and frequency of binge drinking. We compared sociodemographic variables and HIV risk variables by those who partake of hazardous alcohol use (AUDIT score ≥8) against those who do not. A multivariate logistic regression model is presented to determine independent associations with hazardous alcohol use.
Results: Mean AUDIT score was 7.2, median AUDIT was 4.0. Forty percent were determined to be partaking in hazardous alcohol use, 31% drink alcohol at least 2-3 times a week, and a third binge at least once a week. Variables independently associated with hazardous alcohol use were living in Tijuana (adjusted odd ratio [AOR]=5.35, $p<0.001$), ever being in jail (AOR=1.88, $p=0.03$), reporting any sexually transmitted infection (AOR=2.69, $p<0.01$), and having sex while drunk (AOR=4.37, $p<0.001$). It was inversely associated with age (AOR=0.96, $p=0.02$) ever being deported (AOR=5.35, $p<0.001$) and sharing intravenous drugs (AOR=0.45), $p=0.04$).
Conclusions: High rates of hazardous alcohol use among male clients of FSW in Tijuana associated with high-risk sexual behavior. A tailored intervention is needed.
Financial Support: DG and EP are funded thru a NIDA T32 Grant in Substance Use, HIV and Related Infections (DA 023356)

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BIG FIVE PERSONALITY TRAITS AND SMOKING PERSISTENCE OVER 12 YEARS.

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Aims: To investigate the relationships between the big five personality traits (neuroticism, extraversion, conscientiousness, openness, agreeableness) and persistence of regular smoking over a 12 year time span among adults in the United States; 2) To examine evidence of a dose-response relationship between personality traits (e.g., level of neuroticism) and frequency/amount of smoking over 12 years; 3) To investigate whether depression/anxiety disorders mediate the relationships between personality traits and persistence of smoking.
Methods: Data were drawn from the Midlife Development in the United States (MIDUS I; 1994) and MIDUS II (2006), a nationally representative sample which was interviewed in 1994 and then followed up in 2006. Data were collected on the Big Five personality traits (using the NEO-PI), smoking (frequency, amount) and depression/anxiety disorders (using CIDI K-6 scales) at both time points. Logistic regression analyses were used to examine the relationship between personality factors in 1994 and persistence and quantity of smoking from 1994-2006, adjusting for mood/anxiety disorders.
Results: Neuroticism was associated with significantly increased likelihood of persistent smoking from 1994 to 2006 while conscientiousness predicted smoking cessation by follow-up. There was evidence of a dose-response relationship between neuroticism and frequency/amount of cigarette smoking 12 years later. Depression and panic attacks partially mediated the relationship between neuroticism and persistent smoking.
Conclusions: The results of this study add to and extend previous knowledge on the relationship between personality traits and smoking by showing that personality traits are predictive of the persistence of smoking over a 12 year period among adults in the United States. In order for tobacco control efforts to continue to be effective at pushing the prevalence lower, the mental health of smokers may need to be taken into account—both in community-based and clinical intervention programs.
Financial Support: No outside funding.

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GENETIC PREDICTORS OF NEONATAL ABSTINENCE SYNDROME IN METHADONE-EXPOSED INFANTS.

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Aims: Maternal and infant genetic make-up may contribute to inter-individual variability in response to opioids consumed by the mother during pregnancy. This may impact the need to medicate infants to control NAS and their response to medication. This project aimed to investigate the use of genetic markers, *ABCB1* coding for a drug efflux transporter, and *OPRM1* coding for μ opioid receptors, to predict, and attempt to better manage NAS in methadone exposed infants as measured by infant morphine requirement.
Methods: This feasibility study collected cheek cells from 10 methadone maintained mothers during pregnancy and their subsequent newborns following delivery.
Results: Genomic DNA was extracted, with sufficient quantity obtained for *OPRM1* genotyping in all samples, and *ABCB1* haplotyping in seven infants, four of which required morphine treatment. *OPRM1* genetic variability was detected in only one infant, thus statistical analysis was not possible. However, it remains possible that *OPRM1* variants can result in higher opioid dosage requirements as observed previously. For *ABCB1* haplotype, non-parametric analysis showed trends towards infants with variant haplotypes (V, n= 4) requiring lower maximum doses and less total morphine over a four week post natal follow-up period to manage NAS, compared with infants who carried the wild-type haplotype (WT, n= 3), median (range) mg: maximum morphine, WT=0.25 (0-0.30) and V=0.10 (0-0.40); total morphine, WT=23.9 (0-31.5); V=11.4 (0-36.2).
Conclusions: Linking ABCB1 genetic variability and morphine dose may indicate infants with an altered functioning efflux drug transporter require lower morphine doses to control NAS. Consequently, genetic markers may be used as predictive tools to pre-determine NAS severity, leading to better infant management by minimising morphine administration and reducing infant hospital stays. This is preliminary data and therefore collection and analysis for this project continues.
Financial Support: Division of Health Sciences Research Development Grant, University of South Australia.

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SEVERITY, FREQUENCY AND VARIETY OF CRIME IN HEROIN-DEPENDENT PRISONERS ENROLLED IN A BUPRENORPHINE STUDY.

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Aims: This study obtained data on dimensions of criminal activity:severity,frequency, variety, and income from prisoners participating in a buprenorphine study. This paper examined the above dimensions and their relationships with six domains based on the criminal justice and substance abuse literature: demographic characteristics, substance use, criminal behavior, employment, drug treatment, and psychological problems.
Methods: Male and female participants (200) were interviewed in prison. Four sets of analyses were conducted with the criterion variables, with the predictor variables from the domains included in each of the analyses.
Results: Gender (p=.001) and onset of criminal activity (p=.009) were the only significant predictor variables related to crime severity. Males were more likely than females to participate in violent offenses. Individuals who used cocaine more frequently were involved in more criminal activity days (p=.002). Crime variety was related to three predictor variables, gender (p=.001), onset of criminal activity (p=.001), and psychological problems (p=.002). Males were involved in more types of criminal activity compared to females. Participants that began their criminal careers at a younger age were more likely to be involved in a wider variety of criminal activity. Offenders reporting more days of psychological problems were also more likely to be involved in a wider variety of criminal activity. Age of respondent was inversely related to illegal income (p=.011). White participants reported generating more income from illegal means compared to black participants (p=.042).
Conclusions: Results show several important similarities to results on previous cohorts of inmates with histories of heroin addiction, although the present sample may have more of a tendency toward violent crime. Results of this study suggest there are a number of variables that lead further to the understanding of the criminal career paradigm and illustrate the importance of addressing substance abuse and criminal activity.
Financial Support: NIDA1R01DA021579

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THE INFLUENCE OF TRAIT AFFECT ON THE EMOTION-EFFECTS OF ALCOHOL.

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Aims: Previous literature has shown that Positive Affect (PA) and Negative Affect (NA) may be tied to drinking in differential manners. Researches have found that state NA (more short-term emotionality) is predictive of subsequent, lower state NA after drinking while state PA is predictive of subsequent, higher state PA after drinking. However, no studies have examined the impact of both state and trait affect (more durable emotionality) on the emotion-effects of alcohol. By examining both trait and state affect measurements in the current study, we expect that those with high trait PA, when compared to those with high trait NA, will have more increased state PA as Blood Alcohol Content (BAC) increases and will have more decreased state NA as BAC increases.
Methods: Sixty five university students (46% male and 54% female), recruited from local bars and pubs, completed time 1 and 2 measures. At time 1, the researchers measured the participants' BAC and measured state emotional affect through the Profile of Mood States-Shortened Version (POMS-SV), which asked individuals to report on how they were feeling at the current moment. At time 2 (within approximately 48 hours of time 1), participants were given the POMS-SV, which asked individuals to report on their general dispositional affect.
Results: Those with high trait PA experienced differential benefits from alcohol consumption. After controlling for mean age (22.03), we found a significant interaction (b = .38, p = .01) for trait PA and BAC on state PA. As BAC increased, those with high trait PA, but not low trait PA, experienced increased levels of state PA. A marginal association (b = .28, p = .09) between trait NA and BAC on stress was found, suggesting that individuals with low trait NA, compared to those with high trait NA, experienced more decreased stress levels as BAC increased.
Conclusions: Our current study suggests that benefits in positive mood enhancement or negative mood reduction may not occur for those with high trait NA. Future research should look at other pathways to drinking for those with high trait NA, as previous research has supported more cognitively based benefits.
Financial Support: None

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ALTERED PROCESSING OF RISK-TAKING IN THE INSULA PREDICTS RELAPSE IN RECENTLY ABSTINENT METHAMPHETAMINE-DEPENDENT INDIVIDUALS.

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Aims: Evidence in healthy groups suggests the insula plays a critical role in processing risky decisions, where insular activation increases with degree of risk. In contrast, substance-dependent groups have demonstrated disrupted insular risk-processing relative to comparison groups, although it remains unclear how risk-processing differences contribute to outcomes in substance use disorders. The present study examined recently abstinent methamphetamine-dependent individuals (MDI) to test the hypothesis that insular processing of risk may offer predictive value in determining if MDI would relapse or remain abstinent.
Methods: MDI (N=63) were recruited from a treatment program and had ceased using methamphetamine a mean of 28 days prior to participating. MDI performed the risky gains task (RGT) during event-related functional magnetic resonance imaging. During the RGT, individuals could select a "safe" response or a "risky" response that was associated with a higher pay off but also the possibility of a loss. One year after participation, follow-up calls determined if MDI had relapsed (N=18) or were in full remission (N=45).
Results: Behaviorally, the in-remission and relapse groups showed no difference in their selection of risky options. There were no group differences in lifetime methamphetamine use. However, in-remission relative to relapsed MDI showed increased activation during risky decisions and attenuated activation in the bilateral insula during safe decisions.
Conclusions: Whereas in-remission MDI showed a pattern of insular activation early after cessation of drug use similar to what has been described in healthy volunteers, the relapsed MDI did not show differential insula activation during risky versus safe choices. Thus, inadequate processing of risk within the insular cortex may predict who is likely to relapse after cessation of drug use.
Financial Support: This work was supported by the National Institute on Drug Abuse (R01-DA016663, P20-DA027834, R01-DA027797, and R01-DA018307 to Martin Paulus).

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USE OF A SLIDING SCHEDULE ENHANCES COCAINE SELF-ADMINISTRATION IN A HUMAN LABORATORY SETTING: RELEVANCE FOR RELAPSE PREVENTION.

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Aims: Drug self-administration by humans is considered to be a highly predictive laboratory measure for developing mediations to prevent relapse. However, we observed relatively low levels of drug taking under a previously described procedure in which participants chose between receiving cocaine or ascending amounts of an alternative monetary reward. Therefore, we developed a sliding-scale schedule in which cash reinforcement is not available until at least some drug infusions have been self-administered. Afterwards, the amount of cash available is adjusted according to rates of drug taking. The present study was designed to compare cocaine self-administration under the two schedules.
Methods: 13 participants with a history of regular cocaine use were evaluated as they intravenously self-administered 0.46 mg/kg of cocaine or saline using a patient-controlled analgesia pump in a laboratory setting. Prior to self-administration, that dose of cocaine or its placebo was made available noncontingently. For both schedules, drug was delivered under a fixed-ratio-5 contingency.
Results: Under the standard, ascending schedule participants self-administered relatively few infusions per session. Use of the sliding schedule increased the number of self-administered cocaine infusions (3.58 ± 0.34 vs 1.50 ± 1.03, for sliding and standard, respectively). Self-administration of intravenous placebo was also increased under the sliding schedule (4.00 ± 0.61 vs 0.25 ± 0.22). Response latency did not differ across schedules.
Conclusions: The choice of receiving cocaine or an ascending amount of cash supported a relatively low level of drug taking in this group of participants. It was feasible to use of a sliding schedule which initially did not offer an alternative reinforcer, and subsequently controlled its rate of increase. The latter schedule increased self-administration of either cocaine or placebo, and may be more suitable for studies seeking to attenuate drug-reinforced behavior.
Financial Support: Supported by grant R21-DA029787 from the NIH, Institute on Drug Abuse.

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INSULIN, DOPAMINE D2 RECEPTORS, AND MONETARY REWARD DISCOUNTING: A COMMON PATHWAY FOR FOOD AND DRUG ADDICTION.

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Aims: Abnormal brain dopamine (DA) function underlies both food- and drug-reward-related pathology. While animal studies have shown that the pancreatic hormone insulin acts on mesolimbic DA neurons to alter reward sensitivity, and food- and drug-reward behavior, research in human populations is lacking. In this preliminary study, we examined relations among insulin function, DA D2 receptor measurements, and reward choice in humans. We hypothesized that insulin function would relate to DA D2 and reward choice in humans.
Methods: Data from 14 obese (BMI>30 kg/m2; ages 23–41) and 14 normal-weight adults (BMI<28 kg/m2; ages 23–40) were analyzed. Insulin function was derived from an oral glucose tolerance test (OGTT). Central DA D2 receptor binding potential (BP) was computed in a priori reward regions of interest (ROIs) using a D2R-specific, nondisplaceable, positron emission tomography (PET) radioligand, [11C](N–methyl)benperidol (NMB). Reward choice was assessed using the delayed (DRD) and probability (PRD) monetary reward discounting tasks.
Results: Obese and normal-weight participants did not significantly differ in age, D2R BP in any ROI (caudate, putamen, NAcc), or reward discounting (PRD; DRD). D2R BP did not correlate with reward discounting or insulin function within the entire sample, after controlling age, gender, education, BMI and insulin. However, insulin did correlate with DRD (r=.49; p=.02; controlling age, gender, BMI and education), such that better insulin function related to preference for large delayed rewards. Within the obese group, insulin correlated with PRD (r=–.84; p=.005; controlling age, gender, BMI and education), such that better insulin function related to preference for large riskier rewards.
Conclusions: These preliminary data suggest that insulin function relates to risk- and delay-based reward choice in humans, as in both food and drug addiction in animals. A larger sample will be needed to confirm and extend these findings.
Financial Support: NIH R01 DK-085575, 2T32HL007456-26; NIDA 5T32DA007261-20

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DROP-THE-LOSER: AN INNOVATIVE DESIGN FOR A CLINICAL TRIAL OF CITALOPRAM FOR COCAINE DEPENDENCE.

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Aims: Adaptive designs have the potential to change the way clinical research is conducted. These novel study designs can answer the same questions as traditional efficacy trials but with notable advantages in terms of flexibility and efficiency. The drop-the-loser (DTL) design is particularly applicable in trials where there are uncertainties regarding which dose level to test further. This methodological paper describes the planning of a DTL randomized clinical trial of citalopram for cocaine dependence. We present simulation study results used to select pruning criteria and assess the relative merits of this design over a non-adaptive parallel-group design.
Methods: In an ongoing randomized clinical trial, cocaine dependent subjects (target N=125) receive citalopram 20 mg, 40 mg, or placebo in double-blind fashion. An interim analysis planned at 50% of data-gathering will drop or "prune" the active medication dose that is performing least well.
Results: Monte Carlo simulation scenarios were set up to consider a variety of pruning rules for detecting a clinically meaningful effect ("benefit") based on longest number of consecutive cocaine-negative urines. Results suggested that a dose condition be retained if there is > 90% posterior probability of benefit, defined as risk ratio > 1.5. If no effect meets retention criteria, the best performing dose condition would be retained. Under simulated scenarios the adaptive design allocated more subjects to the more promising treatment conditions, i.e., appropriate "pruning", compared to the fixed (non-adaptive) design.
Conclusions: Simulation results give clear information for dropping ineffective doses without undermining the validity and integrity of the trial. Interim analysis of accumulated trial data will be presented at the meeting.
Financial Support: NIDA Grants P50 DA009262, Project 3 (Schmitz)

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FEASIBILITY OF PRISON-BASED OVERDOSE PREVENTION EDUCATION AND PRESCRIBED NALOXONE AT RELEASE.

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Aims: To conduct a feasibility study assessing individual intervention components and outcome measure development in preparation for a prison-based randomized control trial of intranasal (IN) naloxone at release for fatal overdose prevention.
Methods: Sentenced inmates (N=125) within 4 weeks of release with a self reported opioid use history were recruited from the Rhode Island Department of Corrections. Participants viewed a prison-specific video based training addressing opioid overdose prevention, identification and response steps including administration of naloxone. Materials emphasized the need to train others about these steps. Participants nominated at least one individual in the community to receive training and gave an address where prescribed naloxone could be mailed post-release. At a one-month follow-up visit in the community, participants' demonstrated retention of training by responding to a simulated overdose scenario. Outcomes included order, appropriateness, and timed responses to an overdose simulation. Serious adverse events associated with IN naloxone use were also tracked.
Results: To date, most respondent have received their mailed, prescribed naloxone at or soon after release to the community. On average, participants who took part in the overdose simulation scored 11 of 18 correct responses; the average time for IN naloxone administration was 75 seconds, which is similar to times generated from a recent study of paramedic trainees (87 seconds). There have been no serious adverse events associated with IN naloxone in this study.
Conclusions: The prison setting is conducive to IN naloxone training, though ethical and logistical challenges are substantial for a randomized trial design involving naloxone. Incorporating overdose prevention and naloxone dispensing as standard discharge planning should be explored.
Financial Support: NIH R21 DA 029201

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PATTERNS OF RECENT ALCOHOL CONSUMPTION BY RACE AMONG A SAMPLE OF URBAN MEN WHO HAVE SEX WITH MEN.

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Aims: Aim: Research consistently finds that non-Hispanic blacks report lower levels of alcohol use and lower risk of alcohol abuse/dependence than non-Hispanic whites. However, racial/ethnic patterns of alcohol use and abuse/dependence may be different among men who have sex with men (MSM), who have higher rates of alcohol use than men who have sex only with women (MSW). There is a gap in our knowledge about racial differences in patterns of alcohol use and problematic drinking among MSM. The aim of this study is to characterize patterns of alcohol use and problematic drinking by race among a sample of urban MSM.
Methods: Methods: We examined patterns in alcohol use (any use, heavy drinking defined as 3+ drinks/drinking session, binge drinking defined as 5+ drinks/drinking session) and symptoms of problematic drinking among 408 non-Hispanic black and white MSM living in New York City and recruited via modified time-space, venue-based sampling during 2010-12. Problematic drinking was assessed using a count of symptoms endorsed over a 3-question subscale of the AUDIT (failing to do what was expected due to drinking, inability to stop drinking once started, and needing a drink in the morning after a drinking session; α=0.64).
Results: Results: In bivariate analysis, in the 3-months prior to interview, non-Hispanic blacks were less likely to report weekly alcohol use than non-Hispanic whites (39% vs. 64%, $p < 0.001$) and there was a marginally significant difference by race in terms of heavy drinking (54% vs. 63%, $p = 0.075$), but no difference in binge drinking (21% vs. 23%, $p = 0.655$). Non-Hispanic blacks were less likely to report problematic drinking, as defined by endorsing at least one symptom on the AUDIT sub-scale (18% vs. 33%, $p = 0.001$).
Conclusions: Conclusions: This analysis suggests that among MSM, non-Hispanic blacks report less alcohol use and fewer problems related to alcohol use.
Financial Support: New York Blood Center

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THE WOMEN'S RECOVERY GROUP: OUTCOMES FROM A STAGE II TRIAL.

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Aims: The Women's Recovery Group (WRG) Study is a two-site, randomized controlled trial comparing single-gender group therapy (WRG) to mixed-gender group therapy (Group Drug Counseling; GDC) conducted in two outpatient clinics:(1) an academic teaching hospital and (2) a community treatment program. The study was designed to be consistent with usual community practice and implemented in an open enrollment format.
Methods: Participants ≥18 years were included if they were substance dependent and had used substances within the past 60 days. Women were randomized to WRG (n = 52) or GDC (n = 58).Participants were predominately white (95%) and non-Hispanic (99%), with a mean age of 47 years; 88% had current alcohol, 15% cocaine, and 16% opioid dependence;75% had co-occurring Axis I diagnoses. Substance use outcomes were assessed at months 1-6 and month 9 using the Time Line Follow-Back and Addiction Severity Index.
Results: Women in both the WRG and GDC had reductions in mean number of substance use days in-treatment (12.7 vs 13.7 day reductions for WRG and GDC respectively) and post-treatment (11.3 vs 13.2 day reductions at 3 months, 10.3 vs 12.7 day reductions at 6 months); however, there were no significant differences between the two groups (chi-square = 0.92, df = 3, $p > 0.8$). No significant differences were seen in changes in alcohol (chi-square = 4.06, df = 3, $p > 0.2$) and drug composite (chi-square = 0.74, df = 3, $p > 0.8$) scores between WRG and GDC groups.
Conclusions: While there were no significant treatment differences in women's substance use, women in both groups demonstrated clinically relevant reductions in their use during treatment and six-months post-treatment. The gender-focused WRG, designed for women heterogeneous with respect to substance of abuse and co-occurring psychiatric disorders, is effective and can be implemented in an open group format in community treatment programs.
Financial Support: Support provided by NIDA grants R01 DA015434 and K24 DA019855

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EFFECTS OF N-ACETYLCYSTEINE (NAC) VS. PLACEBO MAINTENANCE ON FRONTAL-CORTICAL GLUTAMATE, MOTOR-CORTICAL EXCITABILITY AND COCAINE SEEKING.

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Aims: In preclinical studies, chronic cocaine exposure disrupts glutamate (GLU) homeostasis and elevates relapse-like behavior, which can be reversed by NAC treatment. This clinical study is determining in cocaine dependent volunteers whether maintenance on NAC vs. placebo alters frontal-cortical GLU levels (1H MRS), motor-cortical excitability (transcranial magnetic stimulation), and cocaine seeking.
Methods: Using a within-subject crossover design, each inpatient volunteer is maintained for one week on NAC (1200-mg TID) and placebo (0-mg TID) in random order. Each week, subjects undergo in vivo 1H MRS scanning (single-voxel TE=23ms PRESS; 3T) to measure neurochemistry in medial pre-genual anterior cingulate (mACC) and orbitofrontal (mOFC) voxels, and TMS to measure cortical excitability. Each week, subjects can also work for units of cocaine (10-mg) vs. money ($0.50 vs. $1.50) on a progressive ratio schedule following cocaine-priming doses (110-mg vs. 4-mg).
Results: Interim findings (n=7; planned n=12) indicate that NAC relative to placebo: decreases mACC GLU levels (Means = 9.43 vs. 10.73, p=.046); increases mOFC total creatine (PCr+Cr) levels (9.69 vs. 8.71, p=.094); and increases cortical excitability during a paired-pulse 15-ms condition (GLU-mediated) (3.76 vs. 2.69), Medication X Condition, p=.013). Cocaine breakpoint is elevated with 110-mg vs. 4-mg priming (3104 vs. 1855, p=.069), reduced with $1.50 vs. $0.50 alternative, (19115 vs. 3044, p=.151), but not attenuated by NAC overall (p=.505) although means are in the hypothesized direction in the cocaine-primed conditions.
Conclusions: NAC is decreasing mACC GLU levels (putative reduction of neuronal activity), increasing mOFC PCr+Cr levels (possible reduction in energy utilization), and increasing motor-cortical excitability, but not strongly altering cocaine seeking. Though interim, the results are encouraging in detecting a medication effect.
Financial Support: NIH R01 DA026861 and Joe Young, Sr. Funds (State of Michigan) supported this research.

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DIFFERENCES BETWEEN YOUNGER AND OLDER MEDICAL MARIJUANA USERS FROM A CLUSTER-BASED SAMPLE OF DISPENSARIES IN LOS ANGELES.

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Aims: Surveys of medical marijuana users (MM) typically use convenience samples and lack in-depth information. This survey sought to obtain in-depth information from a survey of MM users from a cluster-based sample of dispensaries in Los Angeles County.
Methods: MM dispensaries were randomly sampled in proportion to their distribution throughout the county, varying survey recruitment days/times to maximize sampling variability. Analyses examined differences between younger (less than 30 years) and older users.
Results: 182 individuals from 13 dispensaries completed the survey. A majority (74%) was male; ages ranged from 17 to 63, mean = 28.4; 44% were white, 26% Hispanic, 13% African American, 6% Asian/Pacific Islander, 11% other. Median age of first marijuana use was 15 and average duration of MM use was about 2.5 years. Reasons for MM use were evenly split between physical health and mental health conditions, and did not differ by age group. Nearly all (91%) believed that use of MM has helped them "very much." Over half (58%) said they used MM in place of Rx drugs for a health problem, with most preferring MM because it is "natural," has less adverse side effects, and is more effective. About one fifth (21%) reported misuse of illicit drugs, 46% reported risky alcohol use, and 44% smoked cigarettes, with higher rates of tobacco use among younger individuals (51% vs. 33%, $p < .05$). Few respondents had ever received drug treatment (n=5) or believed they needed it (n=2). Younger individuals were more likely to be male and Hispanic, and to report that all or most of their friends used MM (57% vs. 30%, $p < .001$). Older individuals reported more psychiatric symptoms (76% vs. 59%, $p < .05$).
Conclusions: Although reasons for using MM did not differ by age, misuse of other substances was not uncommon, and there were differences in health risk behaviors by age. Health interventions targeted at MM users should address these other high-risk behaviors.
Financial Support: Supported by Los Angeles County Department of Public Health, Substance Abuse Prevention and Control Program (Contract PH-000179)

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ADDRESSING TIME-VARYING CONFOUNDING WHEN ASSESSING THE CAUSAL EFFECTS OF CUMULATIVE TREATMENTS FOR ADOLESCENTS WITH SUBSTANCE USE PROBLEMS.

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Aims: Engagement in substance abuse treatment services is among one of the strongest predictors of treatment outcomes. Engagement may be conceptualized as retention in a single treatment episode or continued involvement in multiple treatment programs and modalities over time. Policy decisions to promote engagement require a more nuanced understanding of the causal effects of retention and cumulative effects of multiple treatment episodes.
Methods: We use a marginal structural model (MSM) to examine the causal effects of cumulative treatment experiences over a period of 9 months among adolescents receiving care in community-based treatment settings on drug use at the end of 1-year. During the 9 months, adolescents may move in and out of outpatient, residential, and biological drug screening treatment modalities or may have periods of time where they receive no treatment. We utilize inverse probability of treatment weighting (IPTW) to reduce confounding bias due to observed baseline and time-varying measures over the course of 9 months in treatment. The weights are estimated using generalized boosted models (GBM) rather than parametric approaches. We compare our results to traditional regression analyses.
Results: Each additional episode in a residential facility yielded a 14% decrease on average in 12-month substance use frequency (95% CI = -25%, -3%) relative to no treatment. Each additional episode in an outpatient treatment facility yielded an 11% decrease (95% CI = -23%,-0.01%) and each additional episode of biological drug screening (with no additional outpatient or residential treatment) yielded a 21% (95% CI = -31%, -9%).
Conclusions: We find promising evidence that additional episodes of outpatient and residential treatment as well as biological drug screening lead to increased improvement in substance use outcomes at one year.
Financial Support: NIDA grant 1R01DA015697 (PI: McCaffrey).

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CITICOLINE ALTERS IMPULSIVITY IN MARIJUANA SMOKERS.

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Aims: Citicoline, available as an over-the-counter supplement, plays an important role in cellular metabolism and has been used therapeutically for stroke, traumatic brain injury, and cognitive dysfunction. Previous investigations have reported that citicoline treatment also increases frontal brain metabolism and reduces craving for illicit substances. Impulsive behavior is often associated with substance abuse, and frequently reported as a risk factor for initiation and maintenance of substance abuse. Given this relationship, we examined the impact of citicoline treatment on reported impulsivity levels in marijuana smokers, and hypothesized that treatment may reduce impulsivity in this population.
Methods: All subjects were enrolled in an 8-week placebo-controlled, double-blind trial of citicoline in chronic marijuana smokers. Data was assessed from fifteen subjects; 8 in group A and 7 in group B. Subjects were randomized to receive either 2 grams of citicoline or placebo daily, and were evaluated repeatedly during the 8-week trial. All subjects completed clinical rating scales at baseline and throughout the 8-week treatment period, which included the Barratt Impulsiveness Scale (BIS). The BIS is a robust 30-item, self-report scale that provides reliable measures of impulsivity on three subscales: attention, motor and non-planning, as well as a total impulsivity score.
Results: At baseline, no between-group differences were detected for any of the BIS scores, however, group A demonstrated an overall decrease in BIS scores including attention ($p=.03$) and total impulsivity ($p=.04$) from baseline to week 8 of treatment. Group B showed a significant decrease on the attention subscale of the BIS ($p=.04$), but demonstrated increases on all other BIS scores.
Conclusions: "Breaking the blind" revealed that Group A received active citicoline, while Group B received placebo. Taken together, these data suggest that citicoline reduces impulsivity in chronic, heavy marijuana smokers, which may have treatment implications for other clinical populations with reported difficulty with inhibitory function.
Financial Support: NIDA R01 to Dr Lukas

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HAIR TESTING FOR DRUG USE IN A MODERATE-RISK PRIMARY CARE POPULATION: COMPARISON WITH SELF-REPORT AND EXPERIENCES FROM A CLINICAL TRIAL.

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Aims: To examine experiences with hair testing for drug use implemented as part of a clinical trial of brief intervention for moderate-level drug use.
Methods: This secondary analysis reports data collected at baseline as part of a randomized trial of computerized vs. interpersonal brief intervention with 360 adult participants. Clinic patients at two health centers in New Mexico were screened with the Alcohol, Smoking, and Substance Involvement Screening Tool (ASSIST) for moderate-risk drug use. Hair samples were collected and tested by immunoassays with GC/MS confirmation.
Results: Hair testing results were obtained for over 85% of the baseline sample. Of 360 participants, 20 hair samples (5.6%) were not collected due to participant refusal (10) or insufficient hair (10). Of the 340 samples collected, 300 (83.3%) were from scalp hair, while 40 (11.1%) were from elsewhere (chest, armpit) due to insufficient scalp hair. Depending on the drug, 6.2%-8.5% of samples could not be analyzed due to insufficient hair quantity. Overall concordance with past 3 month self-report on the ASSIST was 88.0% (marijuana), 87.9% (methamphetamine), 85.7% (cocaine), and 76.6% (opiates). However, hair testing correctly identified only 52.6% (142/270) of self-disclosed marijuana users, 65.5% (38/58) of cocaine users, 26.3% (10/38) of methamphetamine users, and 2.7% (2/73) of opioid users. Comparison between quantitative values in hair and self-reported frequency of use will be presented by drug.
Conclusions: Despite challenges in obtaining a sufficient quantity of hair during sample collection, hair testing was feasible to implement and can be a useful biological indicator of drug use in brief intervention studies due to its long detection window. However, hair test results were negative for a substantial number of participants reporting moderate-risk drug use.
Financial Support: NIDA - R01DA026003 (PI Schwartz)

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CURRENT STATE OF U.S. SYRINGE EXCHANGE PROGRAMS: SUCCESS, NEW TASKS, THE FINANCIAL CRISIS AND THE AFFORDABLE CARE ACT.

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Aims: Syringe exchange programs (SEPs) began in the USA in the late 1980s; currently there are 197 active SEPs operating in 32 states, Washington, DC & Puerto Rico. Since the inception of SEPs in the late 1980s in the USA, HIV incidence among persons who inject drugs has declined 80%, & SEPs have evolved into frontline, multi-service health programs for drug users. However, SEPs currently face severe financial pressure.
Methods: We conducted annual surveys of SEPs participating in the North American Syringe Exchange Network (NASEN). The most recent survey was conducted in Spring 2012, covering 2011 program operations including budget information & services offered by SEPs.
Results: 144 (73%) of 197 programs provided 2011 data. SEPs were active in 117 cities in 32 states, Washington, DC & Puerto Rico. 36.9 million syringes were exchanged, & reported budgets totaled $19.3 million, 84% of which came from local and state governments. SEPs provided many additional services including: male condoms (99%), HIV testing (81%), HCV testing (62%), STD screening (47%), naloxone (47%), & referrals to substance abuse treatment (94%). The Affordable Care Act (ACA) could provide reimbursement for these additional services. 75% of programs reported experiencing funding problems in 2011 due to budget difficulties, re-instatement of the ban on federal funding of SEPs, & re-allocation of HIV prevention funds away from IDU transmission.
Conclusions: While SEPs are currently facing severe financial pressure, US SEPs have been able to maintain syringe distribution along with moderate to high levels of additional supplementary services. The ACA may be the most likely source of needed funding, but billing for individual services would require considerable reorganization of programs. The next few years should provide an important test of US policies for providing healthcare to people who use drugs.
Financial Support: amfAR, The American Foundation for AIDS Research, with support from The Elton John AIDS Foundation (EJAF)

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EARLY INITIATION OF ALCOHOL OR MARIJUANA USE AND NONMEDICAL USE OF PRESCRIPTION DRUGS.

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Aims: Early initiation of use of beverage alcohol (EtOH) or marijuana (MJ) is a predictor of multiple risk behaviors among adolescents, but little is known about whether those behaviors are associated with the nonmedical use of prescription drugs (NMUPD). If associations exist, that information could inform substance abuse prevention efforts. This study examined whether early initiation of alcohol or marijuana use was associated with NMUPD.
Methods: Data were collected from a sample of 4,178 students in grades 9 -12 in five high schools. Logistic regression models adjusted for sex, race/ethnicity, and grade were used to estimate the strength of associations between early initiation of EtOH or MJ use (ie, before age 15) and the nonmedical use of prescription pain relievers, depressants, and stimulants. Early initiates were compared to students who initiated use of EtOH or MJ at age 15 or older.
Results: Data were collected from a sample of 4,178 students in grades 9 -12 in five high schools. Logistic regression models adjusted for sex, race/ethnicity, and grade were used to estimate the strength of associations between early initiation of EtOH or MJ use (ie, before age 15) and the nonmedical use of prescription pain relievers, depressants, and stimulants. Early initiates were compared to students who initiated use of EtOH or MJ at age 15 or older.
Conclusions: Early initiation of either EtOH or MJ use is strongly associated with NMUPD. The findings underscore the importance of implementing broadly-focused substance abuse prevention programs at the middle school level.
Financial Support: Grant from Purdue Pharma L.P.

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KETAMINE FOR TREATMENT-RESISTANT DEPRESSION: SUBJECTIVE EFFECTS AND IMPACT ON PLASMA BRAIN-DERIVED NEUROTROPHIC FACTOR.

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Aims: Ketamine produces rapid antidepressant effects in patients with treatment-resistant depression (TRD) however the magnitude of response varies. Studies suggest ketamine's antidepressant activity may relate to peripheral brain-derived neurotrophic factor (BDNF) levels. This study examined if plasma BDNF was associated with ketamine's antidepressant action and whether levels could predict a beneficial outcome. Positive subjective effects were also determined in response to therapeutic doses of ketamine.
Methods: Patients (N=22) with TRD received a single IV ketamine (0.5mg/kg, N=15) or midazolam (0.045mg/kg, N=7) infusion over 40 min. Depression severity was assessed (40min-7 days) with the Montgomery-Asberg Depression Rating Scale (MADRS). Plasma BDNF levels were determined with ELISA. Subjective and dissociative effects were quantified (40min-24hrs) using a visual analog scale (0-10) and the CADSS (Clinician Administered Dissociative States Scale).
Results: BDNF levels were significantly increased ($p<0.05$) at 240min in patients that responded to IV ketamine and highly correlated with MADRS scores at 240min ($r=-0.700$; $p=0.007$) but not following IV midazolam. Responders with higher plasma BDNF levels following ketamine at 240min had lower MADRS scores ($p<0.01$) at 7 days compared to non-responders. "HIGH" and "EUPHORIA" subjective ratings did not differ between treatments. CADSS scores were higher at 40 min, but not 120min, in patients that received ketamine ($p<0.01$).
Conclusions: Plasma BDNF may be a peripheral biomarker relevant to therapeutic response following IV ketamine therapy. The dose of ketamine efficacious for TRD did not exhibit a high abuse liability profile.
Financial Support: Supported with resources and the use of facilities at the Michael E. Debakey VA Medical Center, Houston, TX. NIH/NIMH grant RO1MH081870,UL1TR000067 and NARSAD (SJM).

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USING INCENTIVES TO IMPROVE PAROLEE ATTENDANCE IN COMMUNITY TREATMENT: PRELIMINARY OUTCOMES.

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Aims: This study is a randomized test of the use of incentives to improve treatment utilization among parolees in community treatment. Aims: For parolees who enter community treatment, determine whether providing incentives for attendance results in greater treatment retention. Analyze covariates to better understand factors that influence retention for this high-severity population.
Methods: Parolees who enroll in community treatment are invited to participate; if so, they are consented and randomized to the Attendance Incentive or Information groups. The Attendance Incentive group receives vouchers for attendance using an escalation/reset schedule.
202 subjects were recruited. Of these, 50% are African American, 1% Asian, 28.7% Latino, 8.4% mixed race or other, and 11.9% White. 70% met DSM-IV criteria for ASPD. Kaplan-Meier and Cox regression analyses (SPSS 19) were performed to analyze the length of time to treatment exit.
Results: At 5 months, 25% of the Incentive group was still in treatment compared to 28% of the Information group. Mean days in treatment: Total sample 101 (SD 97.0); Incentive group 97 (SE 8.6), Information group 106 (SE 10.7, $p = .57$). Using Kaplan-Meier Survival analysis, there was no significant difference in time to treatment exit between the Incentive and Information groups. Using Cox regression with covariates of group (Incentive/Information), age, ASPD, impulsiveness (Barratt), age at first arrest, and age of first substance use – only age predicted time in treatment ($p<.01$).
Conclusions: In this preliminary analysis, providing incentives to improve treatment retention was not effective.
Financial Support: Supported by NIDA Grant R01DA025627-01A1

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COMBINING ACTIVE AND PASSIVE ANTIBODY THERAPY TO FACILITATE INITIATION AND LONG-TERM TREATMENT OF METHAMPHETAMINE ABUSE IN A RAT MODEL OF ADDICTION.

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Aims: We hypothesized that by combining loading doses of an anti-METH monoclonal antibody (mAb7F9) with the long acting benefits of active immunization, we could safely and more quickly initiate the protective effects of antibody therapy. A key feature of the approach is the use of a METH hapten protein conjugate vaccine (MCV) that is not neutralized by co-administration of an anti-METH mAb.
Methods: Two groups of male Sprague-Dawley rats (n=8/group) were immunized with 100 μg of KLH-SOO9-METH vaccine (plus adjuvant) followed by boosts at 3, 9, and 15 weeks. Once an immunological memory was established by the week 3 MCV boost, the rats were treated on weeks 6 and 7 with either vehicle or 100 mg/kg of mAb7F9. A third group of rats (n=8) was dosed with mAb7F9 alone at weeks 6 and 7. Serum collected before and after each boost, and after mAb dosing were analyzed by equilibrium dialysis to determine METH binding titers. At weeks 11 and 17, rats were challenged with 0.56 mg/kg METH for determination of METH serum concentrations. Safety was assessed throughout the study by monitoring general health, body temperature and weight. Upon termination at week 17, the rat immunization sites and 8 key organs were assessed for possible adverse effects. Statistical analysis was by one- or two-way ANOVA with Bonferroni's post-tests.
Results: As expected, titers resulting from mAb7F9 significantly ($p<0.05$) overshadowed the active immunization antibody response at weeks 8 and 9. By week 15, the antibody titers in the mAb7F9 only group were significantly lower than the rats receiving MCV alone or MCV-mAb7F9 combination treatment. Indeed by this time point combined MCV and mAb7F9 treatment was not different from active immunization only. The safety assessments showed no problems with any of the treatments.
Conclusions: In a rat model, it is possible to safely initiate high concentrations of anti-METH mAb7F9 at 6 weeks after the start of a MCV immunization protocol, without hindering long-term immune responses.
Financial Support: NIDA U01DA23900 and T32DA022981

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IMPULSIVITY MODERATES THE RELATION BETWEEN AGE AND INCREASES IN ADOLESCENT ALCOHOL USE.

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Aims: Early initiation of alcohol use is detrimental to adolescents' development (Tapert et al., 2006) and can lead to adverse consequences, such as social and school problems, and even fatal injuries. Trait impulsivity contributes to alcohol initiation and use (Nees et al., 2012). In this research, whether impulsivity in adolescence predicted alcohol use one year later was examined.
Methods: The current study examined changes in drinking behaviors in 232 children (46% female) drawn from a larger prospective study, at two time points approximately one year apart. At the first data collection, participants' ages ranged from 12 to 16 (mean = 14, SD = .90). The sample was racially diverse (52% Caucasian, 36% African American, and 12% Other). At each time point, self-reported impulsivity (Imp), sensation seeking (SS) and alcohol use, and behavioral risk-taking were assessed.
Results: Using linear regression, we examined impulsivity, age, and an age by impulsivity interaction, controlling for risk-taking and sensation-seeking, as predictors of change in alcohol use over time. Age predicted changes in alcohol use ($\beta = 2.25$, $t = 2.38$, $p < .05$). Further, the interaction between age and impulsivity also was significant, suggesting that older children with greater levels of impulsivity reported the greatest increases in alcohol use over time ($\beta = 0.53$, $t = 2.49$, $p < 0.05$).
Conclusions: Age predicted increases in adolescent alcohol use over a one year period, and impulsivity moderated this effect. Alcohol prevention strategies should consider a component targeting impulsivity, particularly those targeted to middle-adolescents.
Financial Support: This research was supported by NIDA grant R01 DA018647-08.

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IDENTIFYING AVENUES FOR INTERVENTIONS TO INCREASE CONTRACEPTIVE USE BY OPIOID-MAINTAINED WOMEN.

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Aims: Pregnancy occurs at a high rate in opioid-maintained (OM) women, with more than 50% reporting ≥4 pregnancies vs. 14% in the general population. More than 85% of pregnancies in opioid-using women are unintended, compared to 40% in the general population. Understanding OM women's attitudes toward pregnancy and knowledge about contraceptives will help guide research toward reducing these adverse outcomes. The present study compared such factors between a sample of OM women and a nationally representative sample of young women.
Methods: OM participants were 28 women in opioid agonist treatment screened for participation in an ongoing contraception study. Participants provided demographics, reproductive history and completed a survey from the National Campaign to Prevent Teen and Unwanted Pregnancy.
Results: OM women were age 18-38 with a mean of 12.2 years of education and were typically unemployed (93%). Similar to prior studies, 39% reported ≥4 pregnancies and 73% of pregnancies were unplanned. Knowledge about contraceptives was equivalent between OM women and the nationally representative sample. The groups were also similar in the percentage who believe pregnancy should be planned (68% vs. 78%), but OM women reported less consistent contraceptive use (25% vs. 68%) and fewer endorsed always being protected from unplanned pregnancy (54% vs. 81%). OM women were less trusting of healthcare professionals for contraceptive information (39% vs. 77%) and fewer said that a doctor helped them choose the best birth control (25% vs. 51%).
Conclusions: Importantly, OM women's contraceptive knowledge was on par with results from a nationally representative sample of young women. These preliminary results suggest interventions are needed to help OM women bring their contraceptive use in line with their conception desires and that providing more effective contraceptives in less traditional settings (e.g., substance abuse treatment clinics, needle exchanges) could be beneficial.
Financial Support: Supported by R34 DA030534 and T32 DA007242.

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ALCOHOL, MOODS, AND MALE-FEMALE DIFFERENCES: A SIX-MONTH DAILY PROCESS STUDY USING INTERACTIVE VOICE RESPONSE.

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Aims: The aim of this study is to better understand the predictive relationship in both directions between moods (anger, sadness, or happiness) and alcohol consumption using daily process data among heavy drinkers.
Methods: Design: Longitudinal daily reports of moods, alcohol use, and other covariates such as level of stress, were assessed over 180 days using interactive voice response (IVR) telephone technology.
Setting: During a visit to their primary care office, participants from a rural state were recruited because they reported heavy drinking. After consenting, participants were asked to make daily calls to an IVR system for six months.
Participants: The sample included 246 (166 men, 80 women) mostly Caucasian adults, average age of 46 years, and 66% meeting criteria for alcohol dependence at baseline.
Measurement: Generalized estimating equations were used to model number of alcoholic drinks predicting average mood scores the next day and moods predicting drinks the next day. Significant interactions with gender led to stratified analyses.
Results: Increased alcohol use significantly predicted decreased happiness the next day ($p=0.001$) and more strongly for females than males, while increased anger predicted increased alcohol use the next day for males only ($p=0.001$).
Conclusions: This daily process study challenges the notion that alcohol use enhances positive mood and dampens negative moods the following day. Our findings also suggest a strong association in the opposite direction between anger and alcohol use that is specific to men. Thus, anger interventions may be especially beneficial for males.
Financial Support: This study was funded by the National Institute on Alcohol Abuse and Alcoholism (R01-AA11954 and R01-AA18658) supporting Drs. Rose and Helzer. Dr. Harder's time was supported by the Fogarty International Center and National Institutes of Health (K01-TW008410), Dr. Ayer's time was supported by the National Institutes of Mental Health (RC2-MH089995), and Dr. Naylor's time was supported by the National Institutes of Arthritis and Musculoskeletal and Skin Disease (R01-AR052131).

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NEURAL BASIS OF MODULATING COGNITIVE CONTROL IN YOUNG ADULTS AT RISK FOR STIMULANT DEPENDENCE: FAILURE TO EXPECT WHEN TO STOP.

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Aims: Isolating neuro-cognitive predictors of substance dependence is critical to understanding and preventing addiction. Given evidence of inhibitory control deficits in substance abusers, we examined plausible neural precursors of stimulant dependence in occasional stimulant users (OSU), a population at higher risk for developing dependence. .
Methods: A total of 158 non-dependent OSU and 47 stimulant naïve control subjects (CS) were recruited over a period of 5 years. They completed a Stop signal task while undergoing functional magnetic resonance imaging (fMRI). Importantly, we used a Bayesian ideal observer model to predict individuals' probabilistic expectations of inhibitory demand on a trial-to-trial basis (P(stop)), allowing us to identify group differences specific to Bayesian expectation and prediction error computation.
Results: Despite a behavioral performance similar to CS, OSU had attenuated neural tracking of P(stop) magnitude in several areas, including bilateral medial prefrontal cortex and left caudate. In addition, OSU showed reduced neural tracking of a Bayesian prediction error representing the discrepancy between predicted probability of stop trial and actual stimulus outcome. These reduced differential activations were evident in the dorsal anterior cingulate cortex (ACC) and bilateral insula, and were inversely related to cocaine and prescription stimulant use respectively.
Conclusions: Together, these results are consistent with the notion that OSU may be less efficient in recruiting prefrontal regions to support the computation of inhibitory response prediction and their dynamic adjustment. The degree of stimulant use in these individuals may specifically predict such depressed neural recruitment.
Financial Support: NIDA R01 DA016663 (Martin P. Paulus)

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BUT THEN WHAT? A LONGITUDINAL ANALYSIS OF CHILD CUSTODY ISSUES AND HOW THEY IMPACT FUTURE SUBSTANCE-USING BEHAVIOR AMONG AFRICAN-AMERICAN MOTHERS.

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Aims: African American women are disproportionately involved in the child welfare system. Substance use is often a precursor to custody loss, yet few studies have evaluated the effect of losing custody on a mother's future substance-using behavior. This research fills this gap by examining the influence of African American mothers' custody issues on subsequent substance use (SU) behavior.
Methods: Three custody issue are examined: official custody loss, unofficial custody loss (child living apart from mother but courts not involved), and having an open Child Protective Services case. Using data on 339 African American women, longitudinal random coefficient models analyzed the effects of experiencing a custody issue on mothers' alcohol, marijuana, and other SU in the following six months.
Results: Models showed that experiencing any of the three custody issues predicted an increase in other SU in the six months after the event ($p<.001$), but did not affect alcohol or marijuana use. When separate models were run for each type of issue, official custody loss predicted an increase in alcohol use ($p<.001$), and both official and unofficial custody loss predicted an increase in other SU ($p<.01$, $p<.05$) at follow-up.
Conclusions: These findings demonstrate that a custody issue is predictive of increasing drug and alcohol use among African American mothers, potentially reducing their likelihood of regaining or retaining custody. This study highlights the need to integrate substance abuse treatment into family case plans to improve reunification rates. Additionally, the finding that unofficial custody loss is predictive of increased other SU suggests that community-based prevention efforts could be designed and implemented to intervene before child welfare system involvement becomes necessary.
Financial Support: Research supported by the National Institute on Drug Abuse (R01-DA22967; PI: Oser and F31-DA030061; PI: Harp).

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PLACE AND DRUG CRAVING: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY.

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Aims: Various conditioning theories and substance abuse treatment traditions suggest that place is an important factor in substance use, maintenance, and relapse. The present study uses Ecological Momentary Assessment (EMA) to examine this issue based on self-report of location and craving for heroin, cocaine, and tobacco.
Methods: Outpatient methadone-maintained cocaine and heroin users (N=114) completed self-report measures on handheld devices during prompts provided randomly throughout the day. These reports included ratings of craving on a 4-point scale and reports of location using 12 predefined options. SAS Proc Mixed was used to compare craving ratings based on location.
Results: Compared to any other location, highest average craving was for "at or near cop spot" for cocaine, $F(1,37)=62.13$, $p<.0001$, heroin, $F(1,35) = 14.72$, $p=.0005$, and tobacco, $F(1,36)=5.57$, $p=.0238$. Heroin craving was significantly lower at home than other locations, $F(1,109)=3.95$, $p=.0495$. There was a trend for tobacco craving to be lower at home, $F(1,109)=3.83$, $p=.0529$, but no difference found for cocaine, $F(1,109)=1.02$, $p=.3159$. At another's home, participants reported higher craving for cocaine, $F(1, 79)=35.32$, $p<.0001$ and heroin, $F(1,79)=6.32$, $p=0.0140$, but not for tobacco, $F(1,79)=0.35$, $p=0.5537$.
Conclusions: Preliminary evidence based on self-report of place suggests effects of location on drug craving, particularly for cocaine. These results are unique in using EMA to assess associations between craving and reports of place, but are limited by the use of self-report of places. Future research combining EMA with Global Positioning System devices will address this limitation.
Financial Support: Research supported by the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse and by the Drug Dependence Epidemiology Training Grant (NIDA T32 DA007292) at the Johns Hopkins School of Public Health, Debra Furr-Holden, Director

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GENDER AS A PREDICTOR OF PAST TREATMENT IN DUAL-DIAGNOSED PATIENTS PRESENTING FOR DETOXIFICATION.

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Aims: Studies show that gender is a factor in where dual-diagnosed patients access the health care system, with men more likely to receive substance abuse treatment and women to receive mental health treatment. The purpose of this study was to evaluate past treatment experiences in dual-diagnosis patients admitted for detoxification government. We hypothesized more reported substance use treatment for males and more mental health treatment for females.
Methods: This was a retrospective chart review of all patients admitted to a detoxification unit during four months and who were identified as having acute or unstable psychiatric symptoms. Data were also obtained on demographics prior mental health treatment, prior substance abuse treatment, number of past overdoses and past 12-month substance use.
Results: The charts of 119 male patients and 58 female patients were reviewed. 57% reported prior mental health treatment before the current admission. There was no significant difference between male and female patients with regards to prior mental health treatment or number of prior detoxification, residential or outpatient substance abuse treatments, past year or life-time overdoses nor with regard to homeless status. Female patients were more likely to report past 30-day (chi-squared (1, N=177)=9.791, p=0.002) and 12-month (chi-squared (1,N=177)=5.961, p=0.015) cocaine use. There was a significant relationship between homeless status and prior detoxification admission ($F(1,175)=6.738$, $p=0.010$) and prior residential treatments ($F(1,175)=7.115$, $p=0.006$), but not prior out-patient substance abuse or mental health treatment.
Conclusions: There is no correlation between gender and past engagement in either mental health or substance abuse treatmentin dual-diagnosis detoxification patients. Homeless status plays a greater role in past treatment at some but not all levels of substance abuse treatment. The higher rates of cocaine use in female patients could have implications for further treatment. Prospective studies are needed to determine inplications for follow dual-diagnosis patients after discharge.
Financial Support: None

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OPIOIDS WITH LOWER BRAIN UPTAKE ARE LESS RECOGNIZABLE IN RAT DRUG DISCRIMINATION TESTS AND THUS POTENTIALLY LESS SUBJECT TO ABUSE.

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Aims: Prescription opioids are the mainstay of analgesic therapy, although their abuse is rising to epidemic proportions. A solution to this problem would be to separate opioid analgesia from abuse potential. Drugs that are readily recognized as opioids are considered more prone to abuse. We have tested whether lowering the rate of brain entry of an opioid will make it less recognizable in rat drug discrimination assays.
Methods: Various mu-opioid agonists were assessed for different properties: 1) Potency by receptor binding and elicited-function in vitro; 2) Brain-uptake rate relative to an antipyrine control compound by in-situ brain perfusion; 3) Potential to be recognized as a mu-opioid agonist by rats trained to recognize oxycodone in the drug discrimination assay. Correlations between these parameters were made to establish underlying relationships between them.
Results: The rate of brain uptake and potency of mu-opioid agonists both correlate inversely with the minimum discriminable dose (MDD) in the rat drug discrimination assay. The highest MDD was observed for opioids with dramatically reduced brain uptake rates (between 0.01 and 0.1 relative to antipyrine) compared to commercially used opioids (brain uptake rates between 0.5 and 10 relative to antipyrine).
Conclusions: Opioid agonists that have a high potency against the mu-opioid receptor and which have a high rate of entry into the brain are more likely to be recognized as a mu-opioid agonists. A low MDD is considered to be reflective of potential abuse liability and consequently opioids with low brain entry rates, and thus higher MDD values, may have less abuse potential. Consequently it may be possible to maintain analgesic efficacy and yet reduce the potential for the abuse, by reducing brain entry rate. Mu-opioid agonists with an engineered reduction in brain uptake rate offer a potential approach to achieving this goal.
Financial Support: Nektar Therapeutics

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DIFFERENCES IN CANNABIS WITHDRAWAL SYMPTOMS BETWEEN INDIVIDUALS WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

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Aims: Individuals with attention deficit hyperactivity disorder (ADHD) have greater cannabis use than the general population. Differences in cannabis withdrawal symptoms were examined between cannabis-dependent adults with and without ADHD.
Methods: Treatment-seeking, cannabis-dependent adults with (n=30) and without (n=23) ADHD enrolled in two pharmacotherapy treatment studies completed the Marijuana Quit Questionnaire, a 176-item semi-structured instrument, to assess withdrawal symptoms during their "most serious" (self-defined) quit attempt without formal treatment. Data were analyzed with chi-square Kruskal-Wallis tests for independent samples with statistical significance of two-tailed alpha value $p < 0.05$.
Results: No significant differences between the two groups in sociodemographic or cannabis use characteristics were found. Majority of subjects were male (84%), white (84%), single (67%); average (SD) age 31.2 (10.6) yrs. Age of first cannabis use was 15.3 (3.0) yrs, of first regular use 17.4 (3.9) yrs. In month prior to quit attempt, 71.4% of subjects smoked cannabis at least daily; 97.5% at least weekly. Ninety-five percent of subjects reported at least one withdrawal symptom, most commonly craving for marijuana (68%), initial insomnia (65%), boredom (57%), restlessness (55%), anxiety (51%), angry (49%), and irritability (49%). Non-ADHD subjects were significantly more likely than those with ADHD to report decreased appetite or weight loss (50% vs. 17%, $\chi 2=5.18$, $p=0.023$). 45% of the non-ADHD group met proposed DSM-5 criteria for cannabis withdrawal syndrome compared to 30.4% of the ADHD group.
Conclusions: Results suggest that more severe withdrawal symptoms may not account for higher rates of cannabis dependence among individuals with ADHD.
Financial Support: Supported by the Intramural Research Program, NIH, NIDA (DAG), 5R21DA018221 (ALM-C), 5R01DA026782 (ALM-C), and French Interministerial Mission for the Fight against Drugs and Drug Addiction (EC).

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WORKSHOP TRAINING IN CONTINGENCY MANAGEMENT: INITIAL EFFECTS ON THE ATTITUDES, KNOWLEDGE, SELF-EFFICACY, AND ADOPTION READINESS OF COMMUNITY ADDICTION TREATMENT PERSONNEL.

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Aims: While the efficacy of contingency management (CM) in addiction treatment is well-established, little is known about impacts of training for community-based treatment personnel. This study reports initial impacts of workshop training among staff at a community-based opiate treatment program (OTP).
Methods: OTP staff (N=17) were recruited to participate in a 16-hour CM training workshop, dispersed as four weekly half-day sessions at their clinic, and complete training outcome assessments one week prior and one week following training. Assessments measured positive/negative attitudes, conceptual and applied knowledge, self-efficacy for implementation, and adoption readiness. To account for assessment reactivity, a subsample (n=10) were randomly-assigned to twice complete the pre-training assessment seven days apart. General linear models (GLM) first assessed assessment reactivity in this subsample, and then training impacts in the full sample.
Results: Across outcome measures, GLM effects targeting assessment reactivity were nonsignificant (all p-values >.25) with effect sizes below threshold for educational significance. GLM revealed significant training effects for increases in conceptual knowledge ($p<.001$), applied knowledge ($p<.01$), self-efficacy for implementation ($p<.05$), and adoption readiness ($p<.05$). GLM revealed trends toward significance ($p<.10$) for enhanced positive attitudes and diminished negative attitudes toward CM.
Conclusions: Study findings indicate this 16-hour, on-site staff training robustly improved conceptual and applied knowledge of CM, self-efficacy to implement CM methods, and adoption readiness. Impacts on CM attitudes were in the intended direction, but did not achieve statistical significance in this small sample. Though replication of these findings is needed, promotional efforts for CM may be well-served by offering contextualized workshop trainings for community treatment personnel.
Financial Support: K23 DA025678-01A2

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A COMPARISON OF U.S. MARIJUANA EXPOSURES CALLS TO POISON CENTERS IN STATES WITH AND WITHOUT MEDICAL MARIJUANA LAWS.

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Aims: To determine if legalization of medical marijuana has impacted the rates of marijuana exposure calls into US Poison Centers.
Methods: States legalizing medical marijuana use have increased from 8 in 2000 to 16 in 2010. US Poison Center data on all exposure calls listing marijuana as a substance from 2000-2010 were analyzed. Data were summarized as the rate of calls per population annually by state for intentional and unintentional exposures. Generalized linear mixed modeling was utilized to determine the association of medical marijuana laws on the number of calls per population over time. The model included a time varying indicator for the enactment of medical marijuana laws and year. Yearly state population estimates were obtained from the US Census..
Results: From 2000 to 2010 there were 34,686 intentional exposure calls that included marijuana as one of the substances. Of these 28% (n=9,743) were for marijuana as primary exposure. For unintentional exposures there were 5,040 calls that included marijuana as one of the substances. Of these 65% (n=3,281) were for marijuana as primary exposure. Results indicate that the risk ratio for intentional (1.06; 95% confidence interval 0.90, 3.44 $p=0.4598$) comparing the presence of a medical marijuana law to no law was not significant, however unintentional exposures (1.25; 95% confidence interval 1.16, 1.55 $p=0.0357$) was significant.
Conclusions: This study was unable to find a significant difference in US Poison Center calls for intentional exposures, but did find a significant difference for unintentional exposures in the presence of a medical marijuana law. Results suggest that the rates of unintentional marijuana exposure calls were higher in states with medical marijuana laws. However, this finding may be confounded by higher baseline unintentional exposure rates in the states that enacted medical marijuana laws prior to 2000.
Financial Support: Supported by Rocky Mountain Poison & Drug Center.

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THE INFLUENCE OF REGIONAL LOCATION AND HOMELESSNESS ON SUBSTANCE ABUSE TREATMENT COMPLETION.

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Aims: Previous research suggests that the region of the country in which clients seek substance abuse treatment and their housing status at admission may influence their treatment outcomes. The purpose of this investigation is to examine the influence of regional location, demographics, treatment modality, primary substance of abuse, and homelessness on the likelihood of treatment completion.
Methods: Data were extracted from the SAMHSA 2009 TEDS-D dataset. Independent variables included demographic characteristics, primary substance of abuse at admission, treatment modality, regional location of program, and housing status.US Census divisions were used to define regional locations. Logistic regression analyses were employed to predict the likelihood of treatment completion.
Results: Results indicate that the likelihood of treatment completion increases for older individuals (over 55, OR=1.40), and those whose primary substance of abuse at admission was alcohol (OR=1.44). Treatment completion was less likely for women (OR=0.83), non-whites (OR=0.74), those with less than a 12th grade education (OR=0.80), and heroin (OR=0.48) and cocaine users (OR=0.89). Treatment completion for residential service modalities were twice as high (OR=2.0) as for outpatient settings. The probability of completing treatment was highest in New England (OR=1.71) and the South Central regions (East and West South Central) of the country (OR=1.63; 1.55). Finally, homeless individuals were considerably less likely to complete treatment than domiciled clients (OR=0.70).
Conclusions: The results show that regions vary in their treatment completion rates. In addition, various demographic characteristics, primary drug of choice, treatment modality, as well as homeless status were associated with differences in treatment completion. Further research should examine what factors account for these variations. Treatment effectiveness may be improved by recognizing the various factors that are associated with program completion.
Financial Support: None.

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ASI CHANGES SUSTAINED OVER 12 MONTHS IN TWO CONTINGENCY MANAGED TREATMENTS.

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Aims: We examined changes in multiple life areas, as measured by scores on the Addiction Severity Index (ASI), for those participating in a contingency management (CM) treatment for cocaine-dependent, homeless individuals.
Methods: Half of participants (n=103) were randomized to receive abstinent contingent housing and work/training (CM), and half (n=103) received the same CM interventions plus behavioral day treatment (CM+). Participants completed the ASI at baseline, immediately following active treatment (six months), and at long-term follow-up (12 months). We hypothesized significant improvement in all 7 composite scores from pre- to post-treatment. We also hypothesized the CM+ group would have significantly more improvement than the CM group.
Results: A total of 141 participants had complete follow-up data at 12 months and were used in the analyses. A repeated measures MANOVA was conducted to determine if the two groups differed in improvement across time. There was no significant group X time interaction, $F(12, 128) = 1.360$, $p=.194$, Wilk's $\Lambda=0.887$. Because there were no differences between CM and CM+, they were combined to examine improvement across time. Results indicated significant overall improvement, $F(12, 129) = 4.524$, $p=.000$,Wilk's $\Lambda=0.794$. Graphs of the data show decreases in all areas between baseline and six months but no major changes from six to 12 months. Follow-up one-way ANOVAs showed significant decreases in mean scores for all composite scores except medical status.
Conclusions: Participation in either treatment resulted in significant improvement in employment, alcohol use, drug use, legal status, family/social relationships, and psychiatric status immediately after treatment. These gains were sustained at a 12 month follow-up. That the CM intervention showed significant ASI gains not different from the CM+ group is consistent with the notion a less costly CM intervention may be used successfully as stepped care for many homeless persons with cocaine dependence.
Financial Support: Partially supported by NIDA grant R01 DA11789-04, RTI International and UAB

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DRUG USE AMONG PATIENTS AT PUBLIC CLINICS TREATING SEXUALLY TRANSMITTED INFECTIONS (STI).

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Aims: We examined the substance use of individuals presenting for STI testing and the relationship of substance use to the prevalence of STI.
Methods: 5012 participants were recruited between April and December 2010 among patients seeking treatment at nine public STI clinics. Self-reported alcohol and drug use in the prior 6-months were collected using Audio Computer Assisted Self Interview. Severe drug use was defined by a DAST-10 score >3.
Results: The sample included heterosexual men (38.1%), men who have sex with men (MSM) (27.9%), and women (34%). Most participants (55.2%) reported using an illegal drug in the prior 6 months; over one-fourth (28.7%) reported drug use other than marijuana, and 17.0% reported stimulant use. About a quarter of the sample (24.7%) had DAST-10 scores consistent with severe drug use, and 6.1% reported intravenous drug use (IDU). There were 16.2% of participants who drank to intoxication. Women had higher prevalence of any STI (55.7%) than either males (38.1%) or MSM (37.2%). Amphetamine use was associated with a higher prevalence of STI for MSM. Crack cocaine use was associated with higher prevalence of STI in all groups. Drinking to intoxication was also associated with higher STI prevalence in MSM and women. Current IDU was associated with an increased risk for STI across all three subgroups. Only 6% of the sample reported currently being engaged in substance abuse treatment.
Conclusions: Severe drug use is common in this sample of STI clinic patients and is associated with higher prevalence of STI. Screening for substance use disorders in STI clinics may be an important strategy for expanding appropriate referrals to substance abuse intervention and treatment.
Financial Support: NIH/NIDA Award # RC2 DA028973: HIV Testing and Counseling in HIV Clinics: An Adaptation of CTN0032

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SUBJECTIVE AND REINFORCING EFFECTS OF MODAFINIL IN RATS.

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Aims: Modafinil is a stimulant used to treat narcolepsy. In humans, its subjective effects are somewhat cocaine-like (Rush et al, 2002, Drug Alc Dep; 67:311) and it serves as a positive reinforcer in recreational drug users (Jasinski, 2000, J Psychopharmacol; 14:53).
Methods: We characterized the subjective effects of modafinil in groups of 6-9 female PVG rats trained to discriminate d-amfetamine (d AMF) (0.5mg/kg ip) from saline and its reinforcing potential in groups of 7-9 male Sprague-Dawley rats trained to intravenously self administer cocaine (0.32mg/kg/injection) on a fixed ratio (FR2) schedule of drug reinforcement.
Results: Tested 30 min after dosing, modafinil (50, 100 & 150mg/kg ip) generalized partially to d-AMF (26-75%) at all doses. When tested at 60 min, modafinil (100 & 150mg/kg ip) still partially generalized to d-AMF. Increasing the dose to 200mg/kg ip did not increase modafinil's ability to generalize fully to d-AMF. In rats which robustly self-administered cocaine (17.4+0.4 infusions/session), modafinil (0.17, 0.50 & 1.66mg/kg/injection iv) did not maintain self administration at levels above placebo (mean number of infusions/session: modafinil = 5.0-5.7 versus saline = 4.4-5.1).
Conclusions: Modafinil produces subjective effects in rats that were recognized as somewhat d AMF-like, but modafinil did not serve as a positive reinforcer in this species. The latter result is not definitive because modafinil's limited solubility prevented the exploration of higher doses in the self-administration model. These data agree with observations made in human subjects suggesting modafinil has only weak stimulant and reinforcing properties. The findings are also consistent with our results from the neurochemical and behavioural profiling of modafinil in rats (Rowley et al, this meeting).
Financial Support: Shire Pharmaceutical Development Ltd

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THE ASSOCIATION BETWEEN INCARCERATION HISTORY AND HIV-RELATED DRUG RISK BEHAVIORS.

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Aims: To compare use of alcohol, nasal heroin, crack, speedball, and injection heroin in the last 6 months among never-incarcerated women, recently released women (within the past 6 months), and women with more distal release from incarceration (7 or more months). The presence or absence of a committed sexual partnership (at least 6 months in duration, and partners are married or cohabitate) was examined as a moderator of drug use behaviors.
Methods: A secondary data analysis of women (N = 479; M age = 35.4, SD=9.5) enrolled in the NIDA-funded NEURO-HIV study in Baltimore, Maryland. Participants, recruited via street outreach, advertisements, and participant referral, completed a face-to-face psychosocial interview, including questions about demographics, drug use, and sex history.
Results: Of the 479 women in the sample, 118 (26.8%) had no incarceration history, 63 (13.2%) were released within the last 6 months, and 260 (54.3%) were released more than 6 months ago; 167 (34.9%) had a committed partner, and 305 (63.7%) did not. Women released within the last 6 months reported the highest rates of past 6-month substance use: 65.1% misused alcohol; 65.1% smoked crack; 54% snorted heroin; 44.4% injected heroin; and 31.7% injected speedball. Rates for these 5 drugs were significantly higher compared to never-incarcerated women and women with more distal release: (X^2(1, n=441)=13.07, p=.001), alcohol; (X^2(1, n=441)=16.14, p<.001), crack; (X^2(1, n=439)=11.01, p=.004), nasal heroin; (X^2(1, n=441)=8.49, p=.014), injected heroin; and (X^2(1, n=441)=13.02, p=.001), speedball.
Women without a committed partner were five times as likely (OR=5.09, 95% CI=2.3, 11.29) to smoke crack and four times as likely (OR=4.34, 95% CI=2.03, 9.3) to misuse alcohol as recently-released women with a committed partner.
Conclusions: Results of this study suggest that recently released female offenders have high rates of HIV-related drug use, and the presence of a committed partnership may be protective against some substance use.
Financial Support: This research was funded by NIDA R01 DA14498.

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IMPROVING EFFECTIVE CONTRACEPTIVE USE AMONG OPIOID-MAINTAINED WOMEN.

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Aims: Rates of unintended pregnancy are alarmingly high (85%) among opioid-abusing women, due in part to low rates of contraceptive use. Efforts to reduce barriers to prescription contraceptive initiation among high-risk populations (e.g., incarcerated women) have had some success, but continuation rates leave much room for improvement. Providing financial incentives contingent on adherence with various medication regimens has been efficacious among substance abusers and may have a role to play with regard to prescription contraceptives, especially when combined with barrier reduction.
Methods: Twenty-one opioid-maintained women of reproductive age who did not plan to get pregnant in the next 6 months and were not already using a prescription contraceptive were randomly assigned to either a usual care condition (UCC) or a contraceptive management program (CMP). Participants in the UCC received condoms, Plan B and referral to local providers. Participants in the CMP also received the World Health Organization's contraception initiation protocol, including a free supply of their chosen prescription contraceptive method, and financial incentives for attending 13 follow-up visits over the next 6 months. Point-prevalence prescription contraceptive use at 1, 3 and 6 months was the primary outcome measure.
Results: Results from this ongoing trial indicate significantly more women in the CMP vs. UCC report prescription contraceptive use at the 1 month (73% vs. 22%), 3 month (90% vs. 17%), and 6 month (90% vs. 33%) assessments. Importantly, prescription contraceptive use did not appear to decrease use of condoms. Also, 36% of CMP participants chose to use long-acting, reversible contraceptives (LARCs) during study participation.
Conclusions: Preliminary results suggest the CMP increases prescription contraceptive use and promotes LARC use among opioid-maintained women without decreasing condom use. Further testing of this innovative intervention appears warranted.
Financial Support: NIDA R34 DA030534 and T32 DA007242

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RANDOMIZED TRIAL OF BUPROPION IN METHAMPHETAMINE-DEPENDENT PARTICIPANTS WITH LESS THAN DAILY METHAMPHETAMINE USE.

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Aims: Two previous randomized trials found an effect for bupropion in reducing methamphetamine (MA) use in the subgroup with lower frequency of MA use at baseline. This study aimed to replicate these results by comparing bupropion versus placebo in MA dependent participants with less than daily MA use at baseline.
Methods: MA dependent volunteers reporting MA use on ≤ 29 of past 30 days were randomized to bupropion SR 150mg BID (N=41) or placebo (N=43) and outpatient counseling for 12 weeks. Primary outcomes were the mean treatment effectiveness score (TES, number of thrice-weekly MA-free urine tests provided) for bupropion versus placebo and proportion achieving treatment success (MA abstinence in weeks 11 and 12) for bupropion versus placebo.
Results: The TES for bupropion (mean 16.1, S.D. 12.7) was significantly higher than for placebo (mean 10.6, S.D. 11.2; p = 0.037). More participants on bupropion (29%, 12/41) achieved treatment success than on placebo (14%, 6/43) however the result approached but did not reach statistical significance (p = 0.087). The number needed to treat with bupropion to achieve one additional treatment success is 6.5.
Conclusions: Results of this prospective trial of bupropion among MA dependent participants with less than daily MA use at baseline, combined with similar results from subgroup analyses in two previous trials, suggest bupropion is effective in MA users with less than daily use. A larger trial in less than daily MA users powered to detect a significant difference in treatment success is warranted.
Financial Support: NIDA grants K23 DA023558 to Heinzerling and T32 DA026400 to Shoptaw

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THE RELATIONSHIPS BETWEEN SMOKING ABSTINENCE-RELATED EXPECTANCIES AND ILLICIT SUBSTANCE USE.

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Aims: Smokers who use illicit substances are less likely to quit smoking than those who do not use other drugs. The outcomes that smokers anticipate from smoking cessation (i.e., abstinence-related expectancies) may contribute to differences in smoking cessation success across the continuum of illicit substance use. The aim of this study was to determine if smokers who use illicit substances expect tobacco cessation to exacerbate other drug use, an expectancy that may decrease the likelihood of smoking cessation.
Methods: 507 racially diverse smokers of at least 10 cigarettes/day (mean age = 40.8, 53.3% men) completed the Smoking Abstinence Questionnaire (SAQ; the standard instrument of smoking abstinence-related expectancies), and reported current frequency of marijuana, opiate, cocaine, other stimulant, and depressant use. Responses on the SAQ were compared across non-users, moderate users (monthly or less; 2-4 times/month), and heavy users (2-3 times/week; > 4 times/week).
Results: Compared to non-users, moderate users of marijuana (p = .005, d = .38), opiates (p < .001, d = .60), cocaine (p = .03, d = .27), other stimulants (p = .02, d = .38), and depressants (p < .001, d = .77) were more likely to expect adverse outcomes from smoking cessation, including an increase in drug use. Similarly, compared to non-users, heavy users of marijuana (p < .001, d = .51), opiates (p = .02, d = .46), cocaine (p = .009, d = .58), and other stimulants (p = .004, d = .55) were more likely to expect smoking cessation to occasion adverse outcomes.
Conclusions: The expectation that quitting smoking will increase drug use may represent a significant barrier to smoking cessation among those who also use illicit substances. Although this expectation is consistent with clinical lore, it conflicts with the finding that smoking cessation increases the likelihood of abstinence from illicit drugs. Tobacco interventions should seek to challenge this expectancy.
Financial Support: Supported by R34 DA031936, U01 DA031515-03S1, and FRI internal funds.

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A QUALITATIVE STUDY OF METHAMPHETAMINE USERS' PERSPECTIVES ON BARRIERS AND FACILITATORS OF DRUG ABSTINENCE.

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Aims: To better understand methamphetamine (MA) use patterns and the process of recovery, this study explored facilitators and barriers to drug abstinence from the perspective of adults with a history of primary MA use.
Methods: Qualitative interviews were conducted with a subset (n=20) of individuals who participated in a long-term follow up study of MA use and were MA-abstinent for six or more months. Respondents provided detailed information on why and how they changed from use to abstinence, factors that facilitated abstinence and put them at risk for relapse. A targeted sampling strategy was used to identify a diverse range of participant experiences in terms of gender, age, ethnicity, substance use treatment participation and months of abstinence; 37% were female; the average age was 46.1 (SD=9.5). Audio recordings and transcripts were reviewed for common themes.
Results: Participants reported a range of mild/moderate to intensely destructive problems with MA, including loss of important relationships and profound changes to who they felt they were at their core, e.g., "I didn't realize how dark and mean I was... I was like a different person." Many reported initial abstinence was facilitated by multiple external forces (e.g., frequent drug testing, threat of loss of children, prison, relocation), but sustained abstinence was more often attributed to a shift in thinking and salient realizations about using; e.g., a woman with sustained abstinence indicated that her shift in thinking allowed her to accept help from others, and to listen to her children express how her drug use affected them; she reported, "it's a work in progress... getting my children's trust back."
Conclusions: Findings indicate individualized interventions and multiple, simultaneous approaches and resources were essential in reaching stable abstinence. Understanding long-term users' experiences with MA addiction, relapse, and abstinence can inform strategies for engaging and sustaining MA users in treatment and recovery.
Financial Support: NIDA DA025113

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THE ROLE OF PARENTAL SMOKING IN ADOLESCENT IMPULSIVITY.

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Aims: Research on impulsivity has consistently demonstrated an association with substance use, particularly tobacco smoking. Additionally, adolescents from families with parental smokers are more likely to be tobacco smokers. Thus, it can be hypothesized that adolescent impulsivity may be related to parental smoking as well. Only one other study has investigated parental smoking, however, the current study distinguished between maternal and paternal smoking to investigate their unique impact.
Methods: Participants were recruited for a larger study investigating the effects of body mass index, substance use, and impulsivity. Participants were adolescent and emerging adults. Analyses were conducted to investigate the effects of maternal and paternal smoking (lifetime smoking status) on adolescent performance on a behavioral measure of impulsivity, the delay discounting questionnaire (DDQ).
Results: Results from a between-subjects ANOVA indicate a significant interaction between maternal and paternal smoking status ($F(1,91)=3.938$, $p=.05$) such that if both parents are reported smokers, adolescents are less likely to be impulsive as measured by DDQ performance. However, when only fathers are reported smokers, adolescents are more impulsive and when just mothers are reported smokers, adolescents are more impulsive as well.
Conclusions: A significant interaction between maternal and paternal smoking status suggestst that there is a significant relationship between parental smoking and adolescent impulsivity such that one parent smoking has a significant impact while both parents smoking may serve as a protective factor. Analyses broken down by gender of the adolescent could shed light on the unique findings of the current study, but given limited sample size of the study these analyses could not be run. Future studies should investigate the relationship between adolescent gender, maternal/paternal smoking status, and adolescent impulsivity.
Financial Support: This study was finacially supported by Dr. Sherecce Fields, faculty start-up funds.

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SEXUAL DISCOUNTING AMONG OPIOID-MAINTAINED WOMEN.

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Aims: Opioid-maintained (OM) women are at elevated risk for acquiring sexually transmitted infections (STIs) because they engage in risky sexual behaviors (e.g. multiple partners, trading sex for drugs/money, inconsistent condom use); little has been done to examine the decision-making processes underlying these risks. Our primary aim is to examine the influence of delay discounting on hypothetical condom use among OM women using a novel Sexual Discounting Task (SDT; Johnson & Bruner, 2012).
Methods: OM women (N=24) chose hypothetical sexual partners from a series of photographs and identified which of these partners they thought were: 1) most likely to have a STI, 2) least likely to have an STI, 3) most sexually desirable, and 4) least sexually desirable. Next, participants indicated their perceived likelihood of engaging in unprotected sex immediately vs. sex with a condom available either immediately or after various delays for each of the four hypothetical partners.
Results: When condoms were available immediately, participants reported that they would be more likely to use a condom with the "most likely to have an STI" partner vs. the "least likely to have an STI" partner (95% vs. 67%, $p<.005$). Analyses of indifference points indicated a strong effect of delay in decreasing condom use within all four conditions. Area under the curve (AUC) values normalized relative to likelihood of choosing condom use on the 0-delay trial indicated greater delay discounting in the "most sexually desirable" condition vs. "least sexually desirable" condition (median of .27 vs. .93, $p<.05$). Differences in normalized AUC values between "most likely to have an STI" and "least likely to have an STI" conditions trended toward significance (median of .98 vs. .33, $p=.056$).
Conclusions: Consistent with results observed among cocaine-dependent individuals, these preliminary results indicate the SDT is sensitive to factors that likely influence sexual behavior and condom use (i.e. desirability of a partner & perceived risk of STI) and suggests that delay discounting may contribute to risky sexual behavior among OM women.
Financial Support: Supported by R34DA030534 and T32DA07242 from the National Institute on Drug Abuse

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AMPHETAMINE USE MEDIATES BETWEEN IMPULSIVITY AND ANAL INTERCOURSE.

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Aims: Heterosexual anal intercourse (HAI) is a concern because of the increased risk of HIV transmission by HAI compared to vaginal intercourse. We hypothesized that the association between impulsivity and HAI would be mediated by amphetamine use.
Methods: The data for the current study were collected between 2006 and 2012 at the Center for Behavioral Research and Services in Long Beach, California. This analysis focused on men and women who had an opposite-sex partner in the past 30 days (N=1217). All participants gave informed consent using a consent form approved by the California State University, Long Beach, Institutional Review Board, and were administered the Risk Behavior Assessment (RBA) and the Barratt Impulsiveness Scale (BIS). The RBA gathers information on demographics, sexual behavior, and drug use. It has been shown to have good reliability and validity. The outcome measure was having HAI within the past month. Impulsivity was measured by taking the sum of the BIS items, and the mediator was amphetamine use during sex within the past 30 days. All associations were assessed using logistic regression. This sample was 64% men, 49% Black, 25% White, 17% Hispanic, and the mean age was 39.8 (SD=12.7) years.
Results: The prevalence of HAI was 25% and 14% reported amphetamine use during sex. Impulsivity predicted amphetamine use during sex in men (OR=1.05, 95% CI 1.03-1.07) and women (OR=1.05, 95% CI 1.03-1.07). Amphetamine use predicted HAI when controlling for impulsivity in men (OR=2.11, 95% CI 1.38-3.24) and women (OR=2.48, 95% CI 1.40-4.40), and was a significant mediator of the impulsivity-HAI association for both men (z=2.95) and women (z=2.60).
Conclusions: These results suggest that it is important to consider personality traits when developing HIV prevention interventions and that drug use may mediate the effects of these personality traits.
Financial Support: Award Number R01 DA030234 from the National Institute on Drug Abuse

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SYNTHESIZING OUTCOMES OF EVIDENCE-BASED PRACTICES IN A MULTI-SITE CLINICAL TRIAL FOR WOMEN WITH TRAUMA AND ADDICTIONS.

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Aims: Epidemiologic studies have found that trauma-related disorders are ubiquitous among women in treatment for addictions. Evidence based practices (EBP) for trauma among those with addictions have brought the field to an important stage: examining mechanistic questions such as how, for whom and when EBP's work best and learning how to implement EBPs in community treatment settings. The National Institute on Drug Abuse's Clinical Trials Network "Women and Trauma" study has contributed to this body of knowledge. With over 15 publications, none has yet provided an integrative overview of the findings. This presentation will examine the contribution of this landmark multi-site psychotherapy trial through a review of primary and secondary analyses that highlight important aspects of patient centered outcomes. From 2004-05 in seven treatment programs, the study randomized 353 women into one of two 6-week treatment groups in addition to treatment-as-usual: 1) Seeking Safety, a treatment for substance abuse and trauma, or 2) Women's Health Education curriculum comparison group. Assessments were administered at baseline, weekly in treatment, and 3-, 6-, and 12-months post treatment. In addition to primary and secondary findings, important mediators (e.g., therapeutic alliance, PTSD severity) moderators (e.g., participation in self-help recovery), individual characteristics (e.g., recovery management) and implementation issues (e.g., safety, racial ethnic client-counselor matching, treatment participation) will be discussed from both research and clinical perspectives.
Conclusions: In an era of patient centered outcomes, new methods and creative analytic techniques are essential to maximize findings from clinical trials. Synthesizing the analyses from the Women and Trauma studies will be presented as a model for how to approach interpreting research outcomes relevant to personalized medicine.
Financial Support: This work was supported by the National Institute on Drug Abuse: U10DA13035 (PI: Nunes), DA01025198 (PI: Morgan-Lopez)

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INCENTIVE-BASED TREATMENT FOR PREGNANT SMOKERS.

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Aims: Smoking during pregnancy is a serious U.S. public health problem. More effective cessation interventions are sorely needed. Current treatments often result in < 20% quit rates. Our group developed an intervention wherein women earn monetary incentives (i.e., vouchers) contingent on verified abstinence that results in quit rates of ~ 35%. The intervention also improves birth outcomes. While encouraging, there is ample room for improvements. We conducted a randomized controlled clinical trial with the goal of improving outcomes without increasing the cost of the incentives. We rearranged the schedule of incentive delivery so that more incentives could be earned early in the cessation effort as early success predicts late-pregnancy abstinence. We also increased counseling intensity for all women.
Methods: Women (N = 118) still smoking at start of prenatal care were assigned to usual abstinence-contingent vouchers (CV), revised abstinence-contingent vouchers (RCV), or a noncontingent-vouchers (NCV) control condition where incentives were delivered independent of smoking status. Hypothesis: We hypothesized a graded abstinence outcome: RCV > CV > NCV.
Results: 7-day point-prevalence abstinence was greater in the two incentive conditions vs. control condition at early (CV: 46%, RCV: 41%, NCV: 13%, Chi Sq tests: p = .004) and late (CV: 36%, RCV, 45%, NCV, 18%, p = .03) antepartum assessments, but did not differ significantly between the two contingent-incentive conditions (CV = RCV > NCV). Comparing to prior trials, we saw no indication that greater counseling increases abstinence in the abstinence-contingent incentive condition (CV), although it may in the control condition (NCV).
Conclusions: Results provide further evidence for the efficacy of incentives for increasing abstinence in this vulnerable population. Future efforts to improve outcomes should examine increasing voucher monetary value, especially in those most at risk for poor outcomes (i.e., heavier smokers).
Financial Support: Supported in part by grants R01 DA014028 and T32 DA07242 from the National Institute on Drug Abuse.

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CANNABIS USE MOTIVES AND FREQUENCY OF USE: COMBINED AND DISTINCT ASSOCIATIONS WITH CANNABIS- USE PROBLEMS.

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Aims: Substance use motivations are important for understanding use-related problems. We examined associations between a twelve factor model of cannabis use motives and frequency of use in order to elucidate the features of cannabis use that are associated with cannabis-related problems.
Methods: Participants were 435 university students with past six month cannabis use. Problems were measured with the Rutgers Marijuana Problem Inventory. Motivations were assessed using the Comprehensive Marijuana Motives Questionnaire.
Results: Stepwise entry of all motives indicated that Coping, Social Anxiety, Boredom and Celebration motives were uniquely positively associated with cannabis-related problems (R2 changes = .02-.03, ps< .01). Enjoyment, Celebration and Sleep motives were uniquely associated with higher frequency of use, whereas Experimentation motives were associated with less frequent use (R2 changes = .02-.09, ps< .01). Frequency of use was positively associated with problems after controlling for motives (R2 change = .02, p< .01). Associations between problems and Coping, Celebration and Boredom motives were moderated by frequency of use; motives were more strongly associated with problems at higher frequency of use. This effect was most pronounced for Coping motives, with a stronger association among more frequent users (R2 = .27, p< .01), compared to less frequent users (R2 = .12, p< .01).
Conclusions: These findings evidence the importance of motives in understanding problematic cannabis use. Moderation analyses revealed that associations between problems and Coping, Boredom and Celebration motives were stronger among frequent users. This pattern was particularly evident for Coping motives and suggests that individuals who engage in high levels of coping-motivated cannabis use may be at particularly high risk of encountering problems and thus represent a potentially important target group for interventions.
Financial Support: This research was supported by a grant to from the Social Sciences and Humanities Research Council of Canada to Zach Walsh.

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LACK OF ASSOCIATION OF CANNABIS USE WITH OPIOID OUTCOMES AMONG OPIOID-DEPENDENT YOUTH.

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Aims: Cannabis use is common among opioid-dependent patients, but studies of its association with treatment outcome are mixed. In this secondary analysis supported by the NIDA Clinical Trials Network, the association of cannabis use with opioid treatment outcome is assessed.
Methods: In the main study, participants (N=152) aged 15-21 years were randomized to receive psychosocial treatments and either a 12-week course of buprenorphine-naloxone with a dose taper to zero in weeks 9-12, or a 2-week detoxification with buprenorphine-naloxone. Drug use was assessed by self-report and urine drug screen at baseline and during study weeks 1-12. The association between cannabis and opioid use at weeks 4, 8, and 12 was examined using logistic regression models.
Results: Participants reported a median of 3.0 days (range=0-30) cannabis use in the past month; half (50.3%; n=77) reported occasional use, one-third reported no use (33.1%; n=50), and one-sixth reported daily cannabis use (16.6%; n=25). Median lifetime cannabis use was 4.0 years (range=0-11) and median age of initiation of use was 15.0 years (range 9-21). Neither past cannabis use (age of initiation and use in the month prior to baseline), nor concurrent use, was associated with level of opioid use.
Conclusions: Overall, cannabis use had no association with opioid use over 12 weeks in this sample of opioid-dependent youth. While cannabis use remains potentially harmful, it was not a predictor of poor opioid treatment outcome, as measured by opioid urine drug screens, in this sample.
Financial Support: NIDA K99/R00 DA029115 (Kevin P. Hill, MD, MHS, PI), NIDA K24 DA022288 (Roger D. Weiss, MD, PI), NIDA CTN U10 DA15831 and the Adam Corneel Young Investigator Fellowship from McLean Hospital to Dr. Hill.

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TOWARD QUANTIFYING THE BENEFITS OF SUSTAINED ADDICTION RECOVERY: FINDINGS FROM A NATIONAL PILOT SURVEY.

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Aims: The many costs of active addiction are well documented but little is known of the changes occurring in key life areas as a function of entering and sustaining recovery, or when they occur. Documenting the experiences and benefits of recovery to individuals and to the nation is critical to disseminating the message that recovery is attainable and desirable, and to reducing stigma.
Methods: Cross-sectional online survey conducted in English and Spanish in Nov-Dec 2012. Information collected on demographics, physical/mental health, substance use and recovery history, and 44 items -asked for both 'in active addiction' and 'since you entered recovery'- representing functioning in the work, finances, legal, health, family, social and citizenship domains.
Results: In Pilot data (N= 1,411 of 2,000 target) the gender balanced sample was mostly >50, white non Hispanic, college educated. Half were being treated for a chronic medical condition, 38% for mental health. Most had been addicted to both drugs AND alcohol, had participated in treatment AND in 12-step, and had been in recovery for >3 years; 20% had received pharmacotherapy. In active addiction, most cited negative events (>50%) concerned finances, mental health, school/work performance, and criminal involvement; 50% or fewer had been steadily employed, had had a primary care provider or paid bills on time. Significant functioning improvements in recovery vs. active addiction were noted in all areas, most notably in work/school performance, emotional health, finances, health behaviors, family and civic engagement, and reduced criminal involvement. Analyses will explore findings as a function of gender and recovery stage.
Conclusions: Early findings support the notion that active addiction bears costly consequences to the individual and to the nation while recovery brings improvements in areas where the individual contributes to rather than costs the nation. This underscores the need for research on recovery to identify identify and evaluate recovery support services.
Financial Support: Faces and Voices of Recovery

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INDIVIDUAL INFLUENCES ON CHANGE TEAM MEMBER ATTRITION IN THE CJDATS2 ASSESSMENT STUDY.

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Aims: One focus of implementation science research is to develop organizational change strategies designed to increase the use of EBPPs. Local change teams (LCT) are a common strategy for doing this. The stability of LCT membership influences its effectiveness . The aims of this study were: 1) to describe LCT member attrition and its reasons, and 2) to predict LCT member dropout using organizational and individual differences measures.
Methods: A 4-phase Organizational Process Improvement Intervention (OPII) intervention paired LCTs of criminal justice and community managers and staff with an external facilitator. LCTs completed a needs assessment of practices related to the assessment, case planning, and referral of offenders to community-based treatment. Findings informed process improvement planning and activities for implementing change within the organizations. At baseline, each team member completed the TCU ORC, EBPAS, and a commitment to the change process scale. Facilitators reported on whether, when, and why LCT members did not complete the OPII.
Results: For aim 1, 38% of LCT members dropped out. Member reassignment to other work units or responsibilities was the primary reason, followed by work load complaints. For aim 2, logistic regression analyses showed LCT attrition was associated with stress, burnout, job dissatisfaction, and workplace non-cohesion.
Conclusions: LCT member turnover is a significant factor impacting implementation efforts. Careful selection of team members is recommended to reduce attrition related to job moves. Assessment of members' perceptions of stress, satisfaction, and cohesion can be used to increase retention.
Financial Support: NIDA, SAMHSA, BJA

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LONG-TERM FOLLOW-UP OF MEDICATION TREATMENT WITH AND WITHOUT A BEHAVIORAL COMPONENT FOR OPIOID-DEPENDENT PARTICIPANTS.

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Aims: Recent study findings found that providing behavioral treatment with pharmacotherapy for opioid dependence does not result in improved outcomes. No difference in opioid use or retention was found by behavioral treatment condition provided with sublingual buprenorphine/naloxone (BUP), however it is unclear whether benefits from behavioral treatment may emerge at distal timepoints. This study extends the earlier investigation by examining outcomes after a subsequent medication-only treatment phase, and at Week 40 and 52 follow-up assessments.
Methods: 202 participants were randomized to behavioral treatment condition (Cognitive Behavioral Therapy, Contingency Management, CBT + CM; No Behavioral Treatment) provided with BUP and medication management for 16 weeks; 134 participants (66%) entered a second 16-week treatment phase provided without a behavioral component. Opioid use and study retention were measured through week 52. Opioid use was measured by the TES, the percentage of opioid-negative urine test results over the number of urine tests possible. Retention was measured for each phase and follow-up: 1) dichotomously by whether the participant completed the phase/follow-up; 2) mean number of weeks retained; and, 3) mean # of clinic visits attended.
Results: Baseline comparisons show no demographic or drug use differences across groups. Mean age was 37.0 years, 69% of participants were males, with 52.5% White, 20.3% Hispanic, and 10% Black. Similar to the first treatment phase, no difference in opioid use was found for any subsequent timepoint by treatment group. Likewise, no significant differences were found for any retention measure by treatment group.
Conclusions: These results indicate that including a behavioral component to treatment with BUP does not improve outcomes either during or immediately after the behavioral treatment phase, or after subsequent treatment and follow-up timepoints, suggesting that BUP provided with appropriate medication management may optimize outcomes.
Financial Support: NIDA DA020210

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STIMULANTS AS SPECIFIC INDUCERS OF DOPAMINE-INDEPENDENT SIGMA AGONIST SELF-ADMINISTRATION.

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Aims: Sigma1 receptors (σ_1Rs) are intracellularly-mobile chaperone proteins implicated in several diseases, psychiatric disorders, and substance abuse. A previous study showed that cocaine self-administration (SA) induced dopamine (DA)-independent reinforcing effects of selective σ_1R agonists.
Methods: The present study assessed whether the induction was specific to SA of cocaine compared to the indirect DA agonist *d*-methamphetamine (*d*-MA), the mu-opioid receptor agonist (-)-heroin and the non-competitive NMDA receptor/channel antagonist (±)-ketamine.
Results: Selective σ_1R agonists (PRE-084, (+)-pentazocine) lacked reinforcing effects in drug-naive rats. SA was not acquired in 28 experimental sessions with the opportunity to self-administer either σ_1R agonist. The same exposure to cocaine was sufficient for its SA, after which robust SA of σ_1R agonists was obtained. As with cocaine, SA of the indirect-acting DA agonist *d*-MA induced the reinforcing effects of PRE-084 as well as (+)-pentazocine. In contrast, experiences with food reinforcement, or SA of (-)-heroin or (±)-ketamine were ineffective as inducers of σ_1R-mediated reinforcement (with PRE-084 or (+)-pentazocine). Among cocaine, *d*-MA, (-)-heroin, (±)-ketamine and PRE-084, only PRE-084 SA was antagonized by the σR antagonist BD-1008. Further, only cocaine and *d* -MA were sensitive to the DA receptor antagonist, (+)-butaclamol. In addition, only SA of (-)-heroin was sensitive to the opioid antagonist (-)-naltrexone.
Conclusions: The results indicate that experiences with indirect-acting DA receptor agonists induce reinforcing effects of previously inactive σ_1R agonists whereas reinforcement through different pharmacological mechanisms is ineffective. It is further suggested that induced σ_1R reinforcing mechanisms may play an essential role in treatment-resistant stimulant abuse, suggesting new approaches for the development of effective medications for stimulant abuse.
Financial Support: Supported by NIDA IRP.

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THE THERAPEUTIC WORKPLACE: A BRIDGE TO METHADONE TREATMENT AND DRUG ABSTINENCE FOR INJECTION HEROIN USERS.

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Aims: We assessed whether the therapeutic workplace, an employment-based intervention for drug addiction, can promote enrollment in methadone treatment and drug abstinence in out-of-treatment, injection heroin users.
Methods: Out-of-treatment, injection heroin users were invited to work in the therapeutic workplace for 4 weeks and were encouraged to enroll in methadone treatment. After the 4-week induction period, participants were invited to attend the therapeutic workplace for 26 weeks and randomly assigned to Usual Care Control (n = 30), Methadone (n = 35), or Methadone & Abstinence (n = 33) groups. Usual Care participants could work independent of their methadone treatment status or urinalysis results. Methadone participants and the Methadone & Abstinence participants had to enroll in methadone treatment to work and received a brief pay decrease if not enrolled. Methadone & Abstinence participants were required to provide opiate- and cocaine-negative urine samples to maintain maximum pay.
Results: After 26 weeks, 73%, 77%, and 85% of participants in the Usual Care, Methadone, and Methadone & Abstinence Groups, respectively, were enrolled in methadone treatment. Methadone & Abstinence participants provided significantly more urine samples negative for opiates (73%) and cocaine (61%) than Usual Care participants (43% and 23%, respectively), and significantly more urine samples negative for opiates than Methadone participants (49%). Methadone participants provided significantly more urine samples negative for cocaine (44%) than Usual Care participants.
Conclusions: Although most participants enrolled in methadone treatment, many continued to use opiates and cocaine. Employment-based abstinence reinforcement in the therapeutic workplace was critical in promoting abstinence from opiates and cocaine.
Financial Support: R01DA023864, K24DA023186, and T32DA07209

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ACCESS TO ADDICTION PHARMACOTHERAPY IN PRIVATE U.S. HEALTH PLANS.

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Aims: Medication-based approaches to addiction treatment are a widely endorsed evidence-based practice. An increasing number of medications now are available to treat alcohol and opiate addictions. To understand access to these medications, it is essential to consider the role private health plans may exert through benefit design. Health plans often use cost-sharing and administrative controls, which may impact physicians' prescribing and patients' use of addiction medications. A decade ago, coverage exclusions and assignment to the highest cost-sharing tier were common for buprenorphine, the newest addiction medication at the time. This study explores health plans' current approaches to benefit design affecting addiction medications.
Methods: Data are from a nationally representative telephone survey of private US health plans in 2010 (n = 385, Response rate: 89%). We examined plans' management of naltrexone, extended-release naltrexone, acamprosate, and suboxone and techniques to encourage use of addiction pharmacotherapy. Results are weighted and represent national estimates.
Results: 96% of products covered extended-release naltrexone, and of those, 50% considered it part of the medical benefit rather than the pharmacy benefit. Other addiction medications were commonly covered (acamprosate 91%, naltrexone 99% and suboxone 100%). Prior authorization was common for only for extended-release naltrexone and rare for other medications. Extended-release naltrexone and acamprosate were usually on the most expensive payment tier in terms of patient cost sharing. Health plans used a variety of ways to encourage addiction pharmacotherapy including provider feedback, financial incentives, coverage and consumer cost-sharing mechanisms.
Conclusions: Management techniques and placement on higher cost-sharing tiers were common and may lead to restricted access to effective treatment options for addiction.
Financial Support: Grants from the National Institute on Alcohol Abuse and Alcoholism (R01 AA010869) and the National Institute on Drug Abuse (R01 DA029316).

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LONG-TERM EFFECTS OF BRIEF STRATEGIC FAMILY THERAPY FOR ADOLESCENT SUBSTANCE USERS.

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Aims: Emerging adulthood, a stage of development from age 18 to age 26, is characterized by rapid transitions into new social contexts that involve greater freedom and less social control than experienced during adolescence. This period of development is important because it is characterized by peak prevalence of substance abuse problem and sets a stage for later adult development. Aim: To examine the long term effectiveness of Brief Strategic Family Therapy® (BSFT®) compared to Treatment As Usual (TAU) in the rates of substance use, number of arrests and externalizing behaviors. To determine if the two interventions, delivered to youth at the time when they were adolescents, differentially influenced outcomes during emerging adulthood. Design: 379 of 480 adolescents that participated in the BSFT effectiveness study agreed to be contacted for extended follow ups. Adolescents in the BSFT effectiveness study were randomized to BSFT or TAU
Methods: One- time assessment of Drug Use, Externalizing behaviors, Arrests and incarcerations was conducted using Timeline Follow Back, Adult Self Report and self report respectively. The average number of years between randomization in the original study and the follow-up study was 4.69 (SD = 0.74; Range = 3–7 years). Drug Use, Arrests and incarcerations were examined using negative binomial models and externalizing was examined using linear regression.
Results: BSFT youth had lower incidence arrests and of lifetime incarcerations as compared to youth assigned to TAU (B = -0.33, p = .01; IRR= 0.72,95% Confidence Interval: 0.55, 0.93) and (B = -0.42, p = .04; IRR = 0.66, 95% Confidence Interval: 0.44, 0.98) respectively. BSFT significantly predicted externalizing at follow-up (B = -0.41, p < .05), but was not related to drug use.
Conclusions: BSFT may have sleeper effects in reducing the number of arrests and externalizing problems.
Financial Support: This work was supported by ARRA grant number RC2 DA028864-02

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RESEARCH ISSUES IN EXECUTIVE FUNCTIONING: IMPLICATIONS FOR ADDICTIONS TREATMENT.

Arthur M Horton; Neuropsychology Section, Psych Associates of Maryland, Bethesda, MD

Aims: Recent research has postulated that the crucial elements in executive functioning are monitoring and updating short-term memory, inhabitation of prepotent responses and task-shifting. This poster will discuss research issue proposing a neural network model of executive functioning.
Methods: Past theories related to executive functioning, have focused on frontal lobe functioning to an excessive degree. This poster will discuss research problems and strategies for elucidating executive functioning. In addition, multiple interacting neuroanatomical areas are postulated to sub serve executive functioning skills and will need to be delineated.
Conclusions: Crucial to understanding executive functioning is the association of executive functioning skills with particular brain areas and the important role played by multiple association areas in planning, monitoring and evaluating human behavior, including addictive behaviors. Suggestions for re-conceptualizing drug abuse treatment will be offered.
Financial Support: None

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ARE FORMER PRISONERS WITH DRUG DISORDERS READY FOR MUTUAL-HELP?

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Aims: Substance use disorders (SUDs) are common among community-returning prisoners. Reentry programs recommend that formly-incarcerated individuals attend 12-step groups. However, little is known about this population's 12-step attitudes or behaviors. We compared formerly- to never-incarcerated clients entering SUD treatment on 12-step-related attitudes and attendance.
Methods: Of 321 individuals, 46% (N=153) had no incarceration history, and 54% (N=181) had at least one jail or prison stay. Participants completed baseline assessments (Addiction Severity Index (ASI); Addiction Treatment Attitudes Questionnaire), on which we compared groups. We also compared groups on ASI severity indices (controlling for baseline) and 12-step meeting participation at a 1-year follow-up.
Results: At baseline, the formerly- and never-incarcerated groups did not differ on demographics. The incarcerated group had more severe drug, legal, and employment problems, and less severe alcohol problems. They also had attitudes that were more consonant with 12-step philosophy: commmitment to AA, belief in a a higher power, identification with other addicted people, commitment to abstinence, and intent to avoid high-risk situations. Further, they were more likely to particicpate in 12-step groups during the post-baseline year. At the 1-year follow-up, the two groups did not differ on ASI severity measures with baseline values controlled.
Conclusions: Results support recommendations of reentry programs that formerly-incarcerated individuals with SUDs should participate in 12-step groups. Formerly-incarcerated clients were functioning more poorly at treatment intake, but had attitudes fitting with 12-step philosophy. They were more likely to particpate in 12-step groups over the following year, and achieved reduced drug problem severity that was equivalent to that of clients who had never been incarcerated. Reentry programs for former prisoners should encourage and facilitate 12-step group participation for those with drug use disorders.
Financial Support: Dept of Veterans Affairs Office of Research & Development (CSR&D, HSR&D)

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PHYSIOLOGICAL AND SUBJECTIVE EFFECTS OF WATERPIPE (HOOKAH) SMOKING.

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Aims: In young adults, waterpipe use is often nondaily, a social activity, and widely perceived as healthier to cigarette smoking. As such, waterpipe smoking is affecting a population of otherwise nicotine-naïve individuals who may have never initiated cigarette smoking. The purpose of this study was to evaluate changes in smoking behavior to assess the relationship of smoke exposure with physiological and subjective effects of nicotine throughout smoking sessions in intermittent waterpipe users.
Methods: This study utilized a within subject design with 4 conditions: nicotine conditions were placebo tobacco (0g) and nicotine tobacco (15g); exposure conditions were low exposure (40L) and high exposure (80L). Eligible participants were between 18-30 years old, smoked <3x/week and didn't use any other form of tobacco. 24 participants completed four smoking sessions. Data were obtained at pre-, during, and post-smoking. Physiological measures included salivary cotinine, CO levels, oxygen saturation, heart rate (HR) and blood pressure (BP). Subjective measures included Visual Analog Scales (VAS), Adapted Direct Effects, and QSU-Brief.
Results: During nicotine tobacco conditions, participants smoked longer ($p<.05$), took more puffs ($p<.05$), and inhaled less volume at each puff. There was also significantly more time between each puff, intermittent puff interval, and inhaled volume per puff compared to non-nicotine tobacco. BP significantly changed over time ($F=2.78$, $p=.04$) and across the smoking conditions ($F=6.32$, $p=.02$). HR was also significantly different across the two smoking conditions ($F=7.92$, $p=.01$). Subjective effects of VAS "Headrush" scale indicated an effect of time ($F=10.03$, $p=.001$), nicotine condition ($F=10.21$, $p=.005$), and a significant interaction ($F=7.46$, $p=.002$).
Conclusions: This study provides insight into waterpipe smoking behaviors in the young adult nondependent nicotine population. In particular, the physiological effects (i.e., increased heart rate and blood pressure) in nicotine-containing tobacco suggest hookah smoking may pose health risks.
Financial Support: State of Washington Initiative Measure No. 171 (WSU Alcohol & Drug Abuse Research Program)

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EFFECTS OF A MUTANT BACTERIAL COCAINE ESTERASE ON COCAINE BRAIN LEVELS MEASURED WITH PET NEUROIMAGING IN RHESUS MONKEYS.

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Aims: A long-acting, mutant bacterial cocaine esterase (CocE) has been shown to protect mice from cocaine-induced lethality, inhibit the reinforcing effects of cocaine in rats, and reverse the cardiovascular effects of cocaine in rhesus monkeys. However, the current study is the first to evaluate the effects of CocE on cocaine brain levels.
Methods: PET neuroimaging was performed at the Yerkes Imaging Center on a MicroPET 220 Focus scanner. Uptake of [11C]-labeled cocaine was characterized in a group of 4 rhesus monkeys following a tracer dose (5 mCi) administered as a rapid i.v. bolus. Image acquisition began coincident with the start of the injection and continued for 90 min. Saline or CocE (1.0mg/kg) was administered i.v. 10 min after injection of cocaine. Activity measures were standardized to body weight and dose of radioactivity injected to yield standard uptake values. Regions of interest for time-activity curves included the caudate, putamen and cerebellum.
Results: The average time to peak levels of cocaine was 9.5 min. The washout rate for cocaine in caudate/putamen was 3% per min following saline and 8% per min following CocE. Hence, CocE induced a 3-fold increase in cocaine clearance from brain. Kinetic modeling revealed no change in binding potential for cocaine, indicating that CocE-induced changes in the time-activity curves and brain clearance were due to reduced cocaine concentrations in blood. CocE had no effect on the cocaine analog, RTI-150, which lacks the benzoyl ester linkage of cocaine.
Conclusions: Peripheral administration of CocE rapidly reduces cocaine brain levels and should alleviate or prevent adverse CNS effects. The results further support the development of CocE for the treatment of acute cocaine toxicity.
Financial Support: DA10344(LLH), DA31246(LLH), P51OD011132(Yerkes Center)

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MATERNAL MENTAL HEALTH AND CHILDREN'S INTERNALIZING AND EXTERNALIZING BEHAVIORS: BEYOND MOTHER'S SUBSTANCE USE DISORDER.

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Aims: Maternal substance abuse and mental disorders can have adverse impact on child development. We investigated the impact of maternal mental health on child behaviors based on a long-term follow-up study of mothers and their children approximately 10 years after mothers' admission to drug abuse treatment.
Methods: Mothers were assessed at admission to substance abuse treatment during 2000 to 2002. Addiction severity index was administered at both intake and follow-up in 2009-2011. At follow-up, each mother was asked to assess one target child using the Child Behavior Checklist for ages 6-18 (CBCL). Mothers' mental disorder diagnoses were obtained from the records maintained by the California Department of Mental Health.
Results: About 46% of these mothers had co-morbid mental disorders; 27% had depressive disorder, 15% bipolar disorder, 15% adjustment disorder, 13% anxiety disorder, and 6% psychotic disorder. Of these mothers, more than half had two or more mental disorder diagnoses. The average age of the target child was approximately 11 years old (range 6 to 17). Approximately 22% of target children demonstrated problem behaviors that were borderline or within clinical range (24% externalizing, 16% internalizing). Children were more likely to demonstrate internalizing behaviors if their mothers had co-morbid mental disorders (relative to substance use disorder only, OR=2.5, 95%CI: 1.4-4.7) or family problems (OR=2.4, 95%CI: 1.2-4.5). For externalizing behaviors, only family problems was significant (OR=3.4, 95%CI: 1.9-5.9).
Conclusions: Addressing maternal mental disorders and family problems are important for child wellbeing as these factors were significantly related to emotional and problem behaviors of children of mothers with mental disorder and/or substance use disorder.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

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SYNTHESIS OF 10-FLUOROALKYL-DIHYDROTETRABENAZINES AS POTENTIAL POSITRON EMISSION TOMOGRAPHY- IMAGING AGENTS FOR VESICULAR MONOAMINE TRANSPORTER TYPE II.

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Aims: Vesicular monoamine transporter (VMAT) is critically involved in several neurodegenerative and neuropsychiatric disorders, including substance abuse, Parkinson's disease, schizophrenia, Attention-Deficit/Hyperactivity Disorder, depression, and Huntington's disease. Therefore, in vivo exploration of VMAT by molecular imaging using positron emission tomography (PET) would be valuable for the understanding, diagnosis, and treatment of these neurological and psychiatric disorders. In this report, novel enantiomeric 10-fluoroalkyl-dihydrotetrabenazines were designed and synthesized for the development of potential PET imaging agents for VMAT2.
Methods: The optically pure 10-fluoroalkyl-dihydrotetrabenazine derivatives were prepared from 7-hydroxy-6-methoxy-3,4-dihydroisoquinoline and the VMAT2 binding affinity of target compounds was determined.
Results: The (+)-ligands demonstrated much higher binding affinity for VMAT2 than their corresponding (–)-enantiomers. In the series, several compounds exhibited VMAT2 binding affinity in the low-nM range.
Conclusions: Fluoro-substituted dihydrotetrabenazines were prepared with high VMAT2 binding affinity, and therefore are potential leads for the development of novel 18F-labeled PET tracers for VMAT2.
Financial Support: NSC, ROC (NSC 101-2325-B-002-010) and Intramural Research Program, NIDA, NIH, DHHS.

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ADOLESCENT FISCHER 344 AND LEWIS RATS DIFFER IN MORPHINE-INDUCED TASTE AVERSIONS.

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Aims: Two inbred rat strains (Fischer 344; F344, Lewis; LEW) have been shown to differ in their sensitivity to the aversive effects of morphine. Specifically, F344 rats acquire and express robust morphine-induced taste aversions, whereas LEW rats fail to display such aversions even at high doses and after repeated conditioning. To assess whether such differences are evident in early development, adolescent rats in each strain were assessed for their ability to acquire morphine-induced aversions.
Methods: Adolescent F344 and LEW rats were first adapted to a deprivation procedure whereby fluid availability alternated between ad libitum access and restriction (every 24 h). Once they were reliably consuming water, subjects were given a novel saccharin solution (after 24 h deprivation) and subcutaneously injected with various doses of morphine (0, 3.2, 10, 18 mg/kg). They were than given free access to water for 24 h. This procedure was repeated for four conditioning cycles. Following the last cycle, subjects were given access to water and saccharin in a two-bottle test of the aversion.
Results: Adolescent F344 rats acquired robust morphine-induced taste aversions at all doses tested. These aversions were evident as early as the second exposure to saccharin. On the other hand, adolescent LEW subjects failed to display aversions at any dose (during aversion training or on the relatively sensitive two-bottle test).
Conclusions: Relative to the F344 rats, the LEW subjects were relatively insensitive to the aversive effects of morphine. These differences parallel those previously reported in adult F344 and LEW rats. Although the strain differences in morphine-induced aversions are clearly developmentally stable, the basis for these differences remains to be determined. This differential sensitivity may account for the greater drug intake in the LEW strain relative to the F344 counterpart.
Financial Support: Supported by grants from the Mellon Foundation to ALR and ZEH.

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DELAY DISCOUNTING BY MONKEYS IN A DRUG VS. NON-DRUG CHOICE PARADIGM.

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Aims: The value of a reinforcer decreases as a hyperbolic function of delay to its receipt, a phenomenon referred to as delay discounting. Previous research focused on isomorphic choice for immediate vs. delayed reinforcers of the same type. The present experiments focused on allomorphic choice for immediate cocaine vs. delayed food (Exp 1) and for immediate food vs. delayed cocaine (Exp 2). Our hypothesis was that discounting of either type of reinforcer would be well described by a hyperbolic equation.
Methods: In Exp 1, 6 male rhesus monkeys chose between immediate cocaine (0.0015-0.4 mg/kg/inj) and delayed food (4 or 8 pellets/choice). In Exp 2, 6 monkeys chose between immediate food (1-16 pellets/choice) and delayed cocaine (0.1 or 0.2 mg/kg/inj). Sessions consisted of 4 forced- and 16 free-choice trials (Exp 1) or 2 forced- and 8 free-choice trials (Exp 2). Choices were separated by a 30-min inter-trial interval.
Results: In Exp 1, immediate cocaine choice increased with dose, and food choice decreased with delay to food, such that dose-response functions for immediate cocaine shifted leftward as the delay increased. In Exp 2, immediate food choice increased with amount of food, and cocaine choice decreased with delay to cocaine, such that choice functions for immediate food shifted leftward as delay increased. Discounting functions were well described by a hyperbolic equation (R2 ranged .74-.99).
Conclusions: Delayed reinforcer delivery decreased cocaine and food choice in these allomorphic situations, and both reinforcers were discounted hyperbolically. Within the impulsivity framework based on delay discounting with isomorphic reinforcers, drug abuse is often conceptualized as impulsive choice for more immediate drug over delayed non-drug reinforcers (e.g., health, family, and job). Results from the present allomorphic situations suggest that cocaine choice may be considered impulsive under one set of conditions (e.g., Exp 1), but self-controlled under others (e.g., Exp 2).
Financial Support: This research was supported by grant R01-DA-027666 to WW from the National Institute on Drug Abuse.

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LONG-ACTING INJECTABLE NALTREXONE INDUCTION: A RANDOMIZED TRIAL OF OUTPATIENT OPIOID DETOXIFICATION WITH NALTREXONE VS. BUPRENORPHINE.

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Aims: Opioid dependence continues to be a national epidemic. Current standard treatment involves agonist maintenance with long-acting opioids or detoxification without pharmacologic support. However, antagonist treatment with naltrexone (mu opioid antagonist), which is also available in long-acting injectable form, represents an important treatment option. The aims of this study are to develop procedures for outpatient detoxification which include naltrexone and to compare induction rates onto injectable, extended-release naltrexone (XR-NTX) between groups receiving naltrexone-assisted versus buprenorphine-assisted outpatient detoxification.
Methods: Opioid dependent-participants seeking naltrexone-based treatment were randomized into 2 groups for short-term outpatient opioid detoxification. One group received a 7-day sublingual buprenorphine taper, followed by one week of washout and induction onto XR-NTX on Day 15. A second arm underwent induction onto oral naltrexone as a 4-day ascending taper, followed by administration of XR-NTX on Day 8. Following induction, participants received biweekly behavioral therapy for 4 weeks; substance use, withdrawal and cravings were also monitored.
Results: For this in-progress study, an N of 100 randomized is expected by trial completion. The sample has been primarily white (64%) and black (25%) and male (66%), with a mean age of 40.9 years (SD=13.3). To date, 11 participants have enrolled in the control buprenorphine detoxification arm, and 16 participants in the naltrexone arm. The induction rate onto Vivitrol is 56% (n=9) for the naltrexone-assisted sample and 45% (n=5) for the buprenorphine-assisted sample.
Conclusions: The data from this study suggest that oral naltrexone is an important alternative medication useful in the opioid detoxification process. Participants treated with naltrexone during outpatient detoxification were as successful at completing induction onto depot naltrexone as those in the control buprenorphine-assisted detoxification.
Financial Support: NIDA DA 010746-09A1

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IMMEDIATE AND SIX-MONTH EFFECTS OF PROJECT EX RUSSIA: A SMOKING CESSATION INTERVENTION PILOT PROGRAM.

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Aims: Up to one third of Russian youth have tried a cigarette by 10 years of age; 27% and 19% of 15 year old males and females, respectively, are current smokers; and up to 27% of high school youth are daily smokers depending on region sample and average age. With only one study on tobacco use cessation programming among teens in Russia having been published to date, more research is needed.
Methods: Project EX, an eight-session clinic-based tobacco use cessation program for adolescents, was tested in an experimental pilot trial (n=164). Intervention and control conditions were randomly assigned, nested within recreational summer camps. The evaluation involved pretest, immediate posttest and a six-month telephone follow-up.
Results: At immediate posttest, Project EX significantly reduced future smoking expectation (46% reduction in EX Condition versus 8% in Control, p<.0001), decreased intention to not quit smoking (-5.2% in EX vs. +1.4% in Control, p<.05), and increased motivation to quit smoking (0.72 vs. -0.04, p<.0001). At six-month follow-up, program participants had a higher intent-to-treat quit rate during the last 30 days (7.5% vs. 0.1%, p<.05). For participants who remained monthly smokers at six-month follow-up, Project EX reduced their level of nicotine dependence (-0.53 vs. +0.15, p<.001).
Conclusions: Results of the Project EX implementation trial are promising for motivation enhancement and increasing smoking quit rates among Russian youth. However, further research on teen tobacco use cessation programming in Russia with larger sample sizes, involving other locations of the country, and with stronger research designs is needed.
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MEDICAL MARIJUANA CARDHOLDERS SEEN IN THE EMERGENCY DEPARTMENT.

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Aims: Although the number of individuals who participate in state medical marijuana programs continues to increase, very little is known about how these individuals interact with other aspects of the healthcare system. The present study examines a large sample of Emergency Department (ED) patients to describe the prevalence and characteristics of adults who report participation in state medical marijuana programs.
Methods: Research staff screened a representative sample of 2,049 ED patients in Michigan for participation in a larger brief alcohol intervention trial between February and August 2012. The present study focuses on the self-report by participants that they have ever been issued a medical marijuana card.
Results: Approximately 4.3% (n= 89) of the sample of ED patients reported that they were participants in state medical marijuana programs. The vast majority of these patients (77.5%; n=69) reported that their medical marijuana card was obtained for the management of chronic pain. On average, patients who participated in state medical marijuana programs reported use of marijuana 12.9 (SD=12.7) days out of the past month. Close to 12% medical marijuana patients reported that a physician had refused to provide them with an opioid within the past year.
Conclusions: Adults who participate in state medical marijuana programs represent a small but important minority of patients seen in the ED. It is critical to better characterize the types and quality of care provided to these individual within traditional medical settings.
Financial Support: This project was supported by NIAAA, R01AA018659

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TREATMENT OUTCOMES BY PATTERNS OF METHADONE AND BUPRENORPHINE INDUCTION STRATEGIES: DOES HIGHER DOSE AND FASTER INDUCTION IMPROVE OUTCOMES?

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Aims: Methadone (MET) and Buprenorphine/Naloxone (BUP) induction is a crucial period of opioid addiction treatment. This presentation describes MET and BUP induction trajectories and their association with opioid use, withdrawal symptoms, adverse events and retention.
Methods: : This is a secondary data analysis of an open-label, multi-site, phase 4 study of liver function in opioid dependent subjects treated with MET (n=529) vs. BUP (n=740). MET participants were divided into 3 induction groups according to the maximum dose they received during week 4: 1. Low dose (<55mg, n=121), 2. Moderate dose (60-95mg, n=262) and 3. High dose (≥100 mg, n=66). Group-based trajectory modeling identified 6 distinct BUP induction patterns based on BUP dose changes during the first week: 1. Low dose shifted quickly to moderate (n=217), 2. Low dose shifted gradually to moderate (n=50), 3. Started and remained on low dose (n=180), 4. Moderate dose, shifted to high (n=114), 5. Moderate dose, shifted to low (n=54), and 6. Started and remained on moderate dose (n=111). For the purpose of this study low BUP dose is ≤8mg, moderate is >8mg and ≤24 mg, high is >24mg.
Results: Among the three MET Groups, preliminary results showed MET Group 3 reported the lowest rate of opioid use in weeks 21-24. MET Group 3 had aOR=0.57, p=0.03 relative to MET Group 1. For the BUP condition, participants in Groups 2, 5 and 6 were significantly less likely to report opioid use in weeks 21-24 relative to reference BUP Group 1, with the best results in BUP Group 6 (aOR=0.41, p <0.001).
Conclusions: Findings confirm a relationship between level and speed of dosing characterized by distinctive induction trajectories and opioid use outcomes.
Financial Support: Dr. Jacobs is employed by NIDA/NIH.

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NOT ASHAMED ANYMORE: LONGITUDINAL CHANGES IN BARRIERS TO TREATMENT ENTRY FOR ONLINE TREATMENT SEEKERS.

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Aims: To identify and recruit online treatment seekers and examine their treatment entry-behavior and related barriers over a period of six months.
Methods: Online treatment seekers were recruited through an online SUD treatment finder (www.allaboutaddiction.com/Rehab-Finder) after completing online screening, followed by eligibility determination and an online informed consent. Participants were emailed links to online assessments, delivered via Survey Monkey, to be completed within 24 hours of initial screening and again at one-week, one-month, and six-months following initial screening.
Results: Forty participants were recruited, presenting broad variability in gender (Female = 60%), age (M = 32, SD = 8.6), geography (10 States represented), and drug use (i.e., substance and severity). Reported barriers to treatment entry at baseline replicated previous findings with stigma, cost, and access all presenting as significant barriers. Follow up assessments provided evidence of substantial shifts in barriers with stigma and shame becoming less prominent while cost and access increased in magnitude. Gender, drug use, treatment-entry and past treatment experience were found to be associated with differences in barriers reported.
Conclusions: Treatment-seeking individuals report changes in the reasons for not entering treatment as they progress through the treatment-seeking process. While stigma and shame are substantial barriers at initial seeking they became less important as the treatment-seeking experience continues. Research into the process through which some barriers become less obstructive for treatment entry, and the role that online treatment- and information-seeking play in this process, could help accelerate barrier removal and facilitate earlier SUD treatment entry.
Financial Support: Financial support for the study was provided by the NIDA Center for Advancing Longitudinal Drug Abuse Research (CALDAR) grant 1F31DA025448-01A1

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THE EFFECT OF METHYLPHENIDATE (MPH) ON COGNITIVE CONTROL IN ACTIVE METHAMPHETAMINE (MA) DEPENDENCE USING FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI).

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Aims: MA dependence is associated with cognitive deficits, and has no effective pharmacological treatment. MPH has been shown to improve inhibitory control in health and cocaine abuse. This study aimed to understand the neurophysiological effects of MPH in both active MA-dependent (AMD) and control (Con) subjects performing a cognitive control task
Methods: AMD and Con subjects aged 18-46 years were scanned using fMRI before and after a single oral dose of MPH (18mg) or placebo (PL) (MAMPH n=8; MAPL n=7; ConMPH n=8; ConPL n=10), whilst performing a colour-word Stroop task [Conditions: Congruent (C) and incongruent (I)]. SPM8 and SPSS19 were used for statistical analysis
Results: Response accuracy was significantly different between conditions ($p<0.0001$-C>I). For response times, there was a significant condition*time interaction ($p<0.05$). Post-drug minus pre-drug fMRI results in ConMPH during I condition showed increased activation of inferior parietal lobule, insula and inferior frontal gyrus relative to MAMPH, and of middle and inferior frontal gyri relative to ConPL. MAMPH showed increased activation of inferior occipital gyrus during C condition relative to MAPL. In response to the Stroop effect (I-C), there was increased activation in middle occipital gyrus in the comparison between ConMPH and MAMPH ($p<0.05$)
Conclusions: Different patterns of fMRI activation were observed post MPH and PL. Whilst the role of prefrontal and parietal regions in cognitive control is well established, that of the occipital cortex is less so. Increased activation of visual pathways in AMD post MPH may be necessary to bias selective attention mechanisms towards the task-relevant stimulus feature. The results from this study inform us how MPH acts in the brains of AMD and provide insights for potential behavioural or pharmacological interventions
Financial Support: NZPERF, UoAFDRF, Oakley

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LOWER GABA LEVELS IN THE DORSAL ANTERIOR CINGULATE CORTEX IMPAIR ABILITY TO IGNORE SMOKING-RELATED CUES IN TOBACCO-DEPENDENT VOLUNTEERS.

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Aims: Substance abusers have difficulty ignoring drug-related cues, which contribute to relapse vulnerability. This "attentional bias" towards drug cues translates into an inability to ignore drug-related stimuli that may reflect deficits in brain regions such as the dorsal anterior cingulate cortex (dACC)—a key region in cognitive control and adaptive decision-making. Quantifying relationships between attentional biases to drug cues and disruptions in dACC neurochemistry could be a major breakthrough in identifying neurochemical causes of relapse vulnerability precipitated by drug cues. Gamma-aminobutyric acid (GABA) deficits have been linked to impaired cognition and addictive disorders, so we hypothesized that reduced GABA in the dACC would predict increased attentional biases towards smoking-related cues.
Methods: In 15 nicotine-dependent smokers, we assessed smoking cue attentional bias using the smoking Stroop task and dACC GABA levels using magnetic resonance spectroscopy (MRS). We also measured affective changes due to short-term nicotine withdrawal using the Positive and Negative Affect Schedule.
Results: We found a negative correlation between attentional bias and dACC GABA levels ($r = -0.63$, $p = 0.01$). Smokers with the greatest attentional bias also experienced more negative affect during early nicotine withdrawal ($r = 0.77$, $p < 0.001$).
Conclusions: Our findings revealed a relationship between heightened reactivity to drug cues and both reduced dACC GABA and early withdrawal symptoms. Because reduced GABA function in frontal brain regions disrupt cognitive function, our findings suggest that smokers with diminished dACC GABA may lack the cognitive resources to successfully ignore highly salient distractors such as tobacco-related stimuli and therefore might be more prone to cue-induced relapse. This newly discovered relationship between reduced dACC GABA and attentional bias provides evidence for a novel neurochemical target for future smoking cessation treatment strategies.
Financial Support: This work was supported by the NIDA Grant K01DA029645.

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THE IMPACT OF STRESS AND TRAUMA ON METHADONE-ASSISTED TREATMENT AND INITIAL TREATMENT ENGAGEMENT IN OPIOID DEPENDENCE RECOVERY.

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Aims: Opioid addiction contributes substantially to morbidity, mortality, and crime in the US. While studies have supported its efficacy, the process of induction onto MAT is psychologically and physiologically stressful with morbidity/mortality rates related to treatment participation and outcomes. Chronic stress may be detrimental to ITE due to its relationship with concomitant affective disorders including post-traumatic stress disorder (PTSD). This prospective study is designed to examine whether levels of stress and PTSD symptomatology negatively impact ITE.
Methods: Intake trauma screening via the PTSD-checklist was performed on 63 individuals seeking outpatient MAT. A subset of the study population (n=28) was administered the Cohen et al. Perceived Stress Scale (PSS).
Results: Within these subjects, 26% and 50% of scores fell within the established recommendations for PTSD screening (>36) and diagnosis (>44) respectively, suggesting a significant trauma background. PTSD scores positively correlate with intravenous drug use $r=.323$, $p<.05$, ASI assessed psychiatric severity $r=.515$, $p<.001$, as well as depression by BDII $r=.475$, $p=.014$, QIDS $r=.375$, $p=.025$, and MAACL $r=.452$, $p=.023$ assessment. Results indicate that sample PSS scores are significantly higher than the established norms $t(27)=5.605$, $p<.001$. PSS scores correlate with a history of benzodiazepine use $r=.450$, $p=0.036$, marijuana use $r=.507$, $p=.016$, as well as ASI psychiatric and PTSD symptom severity $r=.431$, $p=.05$ and $r=.401$, $p=.034$, respectively. Furthermore PSS scores were inversely related to measures of attendance/ITE: percent of IOP sessions attended $r=-.47$, $p=.015$, percent of missed medicating days $r=-.440$, $p=.036$, as well as fewer opioid-free urine drug screens $r=-.349$, $p=.081$.
Conclusions: Stress and trauma clearly impact the psychological state of patients during the initial transition onto MAT. This work will potentially lead to more efficacious interventions for the prevention of stress-related MAT drop-out and relapse in this vulnerable population.
Financial Support: None

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THE EFFECTS OF A LOW AND ESCALATING DOSING REGIMEN OF METHAMPHETAMINE ON SPONTANEOUS BEHAVIORS OF RHESUS MACAQUES (*MACACA MULATTA*).

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Aims: Meth use has many negative psychological and behavioral consequences. Previous research on animals with single or multiple high dose (eg. 40 mg/kg) administrations demonstrated behavioral deficits involving learning and conditioning. However, little research has examined the effects of Meth on spontaneous behaviors under a dosing regimen closer to the human drug-use pattern. The current study examined the behavioral consequences of Meth on spontaneously occurring behavior in three situations in rhesus monkeys that were given a more human-like administration regimen.
Methods: Twelve of 22 adult male rhesus macaques were injected intramuscularly with Meth on weekdays with an escalating dosing regimen starting from 0.1mg/kg and ending with 0.75mg/kg at the end of a four-week period. Ten controls received saline. Behaviors were measured in three settings: the animals' home cages, during a Human Intruder test, and during a Novel Object test. Behaviors recorded reflected the domains of activity, abnormal behavior expression, emotionality, curiosity, and impulsivity. Data were analyzed using a generalized linear model.
Results: Compared with controls, Meth animals showed more activity in the Homecage observation ($p < 0.05$) and in the Novel Object test ($p < 0.01$); demonstrated more abnormal behaviors in the Homecage observation ($p < 0.05$) and Novel Object test ($p < 0.01$); appeared to be more emotionally reactive in the Human Intruder ($p < 0.05$) and the Novel Object tests ($p < 0.01$); and appeared more curious in all three tests. No difference was found in impulsivity.
Conclusions: Under a dosing regimen mimicking a human Meth use pattern, our data showed that, even in the first month at low dose, Meth treatment affected several domains of spontaneous behaviors of rhesus monkeys. In particular, Meth animals showed more curiosity overall and during challenging conditions, the animals responded more emotionally. These findings further clarify the behavioral consequences of Meth exposure.
Financial Support: DA024441, RR000169

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EN UNA PIPA TE CABE TODA TU VIDA: ACCESSING CRACK USERS IN MEXICO CITY.

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Aims: Crack use is increasing in Mexico DF. Researchers at the Instituto Nacional de Psiquiatría and the University of Southern California are conducting a qualitative study in three high-risk districts (Iztapalapa, Cuauhtémoc, Coyoacán) in DF that examines the emergence, adoption, transmission and maintenance of crack use practices among current crack using adults. This presentation describes the methods and challenges to identify, contact, and interview active crack users to successfully conduct this research. The presentation describes how the research team used a variation of adaptive sampling methodology, in combination with elements of field-intensive outreach, Rapid Assessment for Response and Evaluation, and respondent-driven sampling. The field team has completed five months of ethnographic observations and interviewed 133 adults.
Conclusions: Crack users in DF are a hidden population, often operating in closed networks and dangerous communities that are inaccessible to outsiders. There are many challenges to conducting research in high-risk neighborhoods such as recruitment of participants and safety of field workers. Incorporating field workers with previous experience with these high risk populations or indigenous to these communities is essential. Highlighted is the importance of key informants from local neighborhoods who are critical to helping field workers gain access to high risk communities and important gathering places such as parks, alleys, altars, and fumaderos (smoking rooms), which are the scenarios for symbolic and practical interchanges among consumers. Field workers learned to use culturally-specific terms and communication styles to interact and communicate with locals and they needed to be able to maintain trust and rapport with participants by demonstrating their knowledge of street language, learned through their direct experience as indigenous to the sites.
Financial Support: International project funded by the NIH/NIDA, grant: 5R21DA031376-03.

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GENDER DIFFERENCES IN RISK PERCEPTIONS OF VERY LOW NICOTINE CONTENT CIGARETTES.

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Aims: To examine gender differences in risk perceptions of reduced nicotine content cigarettes.
Methods: Subjects smoked 0.05 mg nicotine yield or 0.3 mg nicotine yield cigarettes for 6 weeks prior to a quit attempt under double blind conditions. Smokers rated perceptions of their preferred cigarette at baseline and their study cigarette at weeks 2 and 6, namely the risk of developing lung cancer, heart disease, emphysema, stroke, bronchitis, or other cancers from the cigarette. Subjects also reported perceived addictiveness of the cigarettes. Analyses controlled for perceived risks of the preferred cigarette, age, and changes in cigarettes per day from baseline.
Results: Women smoking the 0.05 mg cigarettes (n=20) reported lower overall health risk from the study cigarette than men (n=20) at week 2 (p=.02). Specifically, women reported lower lung cancer (p=.02), emphysema (p=.03), heart disease (p=.008), and stroke (p=.02) risk from the study cigarette. By week 6, there was a marginal effect of gender on average disease risk (p=.06), while women (n=16) reported significantly lower risk than men (n=17) for lung cancer (p=.03) and bronchitis (p=.03) (stroke and emphysema risks were marginal with p=.08 and p=.06, respectively). Women also perceived the study cigarette to be less addictive than men at week 2 (p=.002); this effect failed to reach significance by week 6. In contrast, no significant gender differences in perceived risk of any disease or addiction were observed during the use of the 0.3 mg cigarettes.
Conclusions: Women may be more susceptible to false notions that very low nicotine content cigarettes are less harmful and perceive them as less addictive during initial weeks of use. This gender effect is specific to cigarettes with very low nicotine delivery. Nicotine reduction strategies aiming to reduce cigarette addictiveness by drastically reducing nicotine content should consider potential gender differences in risk perceptions which may have important implications for smoking behavior, quit intentions, and harm.
Financial Support: NIDA U54DA031659, P50DA013333

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THE IMPACT OF SLEEP DISTURBANCE ON CANNABIS QUIT ATTEMPTS.

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Aims: Although sleep disturbance is commonly rated as one of the most severe cannabis withdrawal symptoms, little is known about the extent, nature and impact of sleep disturbance experienced by dependent cannabis users, and the potential impact about quit attempts. The sleep disturbance experienced by a sample of treatment-seeking cannabis users before, during and after admission to an inpatient withdrawal unit was investigated.
Methods: Cannabis dependent adults (N=38) were admitted to an inpatient withdrawal unit for seven days, and followed up at 14, 30 and 90-days post discharge. The Athens Insomnia Scale was administered at admission and at follow-up. During inpatient admission participants completed a daily sleep diary and wore an accelerometer (Actiwatch 2) to gather objective data on patterns of sleep behaviour.
Results: Nearly three-quarters (74%) were classified as having insomnia in the week prior to admission. Sleep disturbance was commonly experienced during withdrawal, although quality of sleep improved over time (Wald Chi-Sqaure=6.029, p=0.014). Two-thirds (68%) of participants used Nitrazepam on at least one night during admission, although Nitrazepam was not associated with improved quality of sleep. The relationship between sleep disturbance and cannabis use at follow-up will be examined.
Conclusions: Sleep disturbance is commonly experienced by dependent cannabis users, both prior and during withdrawal attempts. Appropriate assessment and interventions may lead to increased likelihood of successful cannabis quit attempts.
Financial Support: Research supported by National Health and Medical Research Council Project Grant (556301).

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ADAPTING A WOMEN-CENTERED INTERVENTION FOR INJECTION DRUG USERS IN THE REPUBLIC OF GEORGIA.

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Aims: Does an integrated women-centered intervention for drug dependence and HIV prevention reduce drug- and sex-risk behaviors of drug-using Georgian women to a greater extent when paired with proactive counseling than paired with case management?
Methods: Interventions were adapted using a mixed-methods approach. 55 drug-using Georgian women and 34 Georgian health care provider interviews underscored the need for a non-judgmental, women-centered drug dependence intervention focusing on employment, life skills, healthy relationships, and HIV and interpersonal violence risk reduction. Using these findings and feedback from US, Georgian and Russian collaborators, and Community Advisory and Beneficiary Advisory Boards, women-centered drug-treatment (Reinforcement-based Treatment) and HIV prevention (Women's Co-Op) approaches were tailored to yield integrated women-centered interventions with proactive counseling or case management. A pilot randomized trial assigned injection-drug-using women to receive either 12 sessions of the proactive counseling (n=10) or case management (n=10). Analyses: Qualitative interview theme coding was done with nVivo. Inferential trial data analysis used a linear mixed model.
Results: Interview findings indicate drug use was more problematic for women than men. Women were seen as failed daughters, wives, and mothers. Providers were less tolerant of drug-using women than men. Pilot trial results showed women in both conditions reduced use of opioids, stimulants, and sedatives, and drugs before sex, and increased use of condoms (all ps<.05).
Conclusions: Women-centered treatment approaches improve the lives of injection-drug-using women in Georgia.
Financial Support: Supported by NIDA grant R01DA029880

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AN OBJECTIVE STUDY OF CONCOMITANT DRUG USE AMONG HEROIN AND PRESCRIPTION OPIOID ABUSERS.

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Aims: Urine drug testing can provide objective information regarding the use of licit and illicit drugs. To better understand the patterns of concomitant drug use among heroin and prescription opioid (ab)users in the New York City (NYC) area, we examined urine drug test results of individuals screening for multiple studies with the Opioid Research Laboratory.
Methods: Following a telephone interview, potential study participants were scheduled for further in-person screening. Standard screening procedure includes an 11-panel urine drug test at each visit. Descriptive analyses and Chi-square tests were used to assess and compare drug use.
Results: In all, urine toxicology results from 266 individuals were included in the analysis. The participants were primarily male (84%), and consisted of intravenous heroin users (42%), intranasal heroin users (32%) and prescription opioid users [23%; a small percentage of heroin users reported both intravenous and intranasal use (3%)]. During screening, 94% of heroin users tested positive for opioids, 33% of these individuals provided at least one urine sample that was also positive for cocaine, 30% for methadone, 23% for buprenorphine, 20% for benzodiazepines, 14% for tetrohydrocannabinol (THC) and 13% for oxycodone. Among prescription opioid users screened, 35% tested positive for opioids on at least one occasion, 33% provided at least one urine sample that was positive for THC, 32% for cocaine, 23% for oxycodone, 10% for methadone, 8% for benzodiazepines and 3% for buprenorphine. Overall, 80 of 206 heroin users (39%) provided a urine sample that tested positive for a non-opioid drug, with a similar ratio being found among prescription opioid users (20 of 60; 33%).
Conclusions: The present study indicates that the use of multiple psychoactive drugs of various classes may be typical for most opioid users. As such, researchers, treatment providers and harm reduction specialists should address the potential dangers of polydrug abuse within this population.
Financial Support: Supported by NIDA grant DA030446 to JDJ.

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THE DISCOVERY OF THE FIRST OPIOID PAN ANTAGONIST WITH NANOMOLAR AFFINITY AT MU, DELTA, KAPPA, AND NOCICEPTIN OPIOID RECEPTORS.

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Aims: The trans-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine scaffold is a known pharmacophore for antagonism at mu-opioid (MOP), kappa-opioid (KOP), and delta-opioid (DOP) receptors, however; its pharmacological activity at the nociceptin opioid (NOP/ORL-1) receptor has not been explored. One derivative based on this scaffold is the selective KOP antagonist JDTic, (3R)-7-hydroxy-N-((1S)-1-{[(3R,4R)-4-(3-hydroxyphenyl)-3,4-dimethyl-1-piperidinyl]methyl}-2-methylpropyl)-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide. In our laboratory, we discovered that JDTic has significant binding affinity at the NOP receptor (Ki 16.67 ± 0.76 nM), with no intrinsic activity in the [35S]GTPγS functional assay. Although the crystal structure of JDTic complexed with KOP was recently reported, its binding conformation at the NOP receptor is currently unknown.
Methods: Thus, in order to explore the structural determinants of JDTic binding for the KOP receptor versus the NOP receptor, we performed rational chemical modifications of this scaffold, leading to a tractable structure-activity relationship (SAR) for modulation of affinity at NOP.
Results: Interestingly, removal of the two dimethyl groups of the trans-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine portion of JDTic allowed for a 10-fold increase in binding affinity at the NOP receptor (Ki 1.75 ± 0.74 nM) while maintaining comparable affinity for KOP, MOP and DOP receptors (Ki 1.14 ± 0.63 nM, 1.67 ± 0.6 nM, 19.6 ± 1.3 nM, respectively). This 4-(3-hydroxyphenyl)piperidine analog AT076, functions as a pan antagonist in [35S]GTPγS assays at all four opioid receptor subtypes. Another antagonist at MOP, DOP and KOP receptors based on a similar scaffold is the trans-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine derivative LY255582, however; its activity at NOP has not been reported.
Conclusions: Herein, we report the first pan antagonist, with potent nanomolar affinity for all four opioid receptor subtypes.
Financial Support: This work is supported by grant R01DA027811 (NZ).

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TESTING FOR AMPHETAMINE-TYPE STIMULANT (ATS) USE TO ASCERTAIN VALIDITY OF SELF-REPORTED ATS USE AMONG YOUNG FEMALE SEX WORKERS IN CAMBODIA.

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Aims: To assess concordance between self-reported amphetamine-type stimulant (ATS) use and toxicology results among young female sex workers (FSW) in Phnom Penh, Cambodia.
Methods: Cross-sectional data from the Young Women's Health Study-2 (YWHS-2), a prospective study of HIV and ATS use among young (15 to 29 years) FSW in Phnom Penh, Cambodia, was analyzed. The YWHS-2 assessed sociodemographic characteristics, HIV serology, HIV risk, and ATS use by self-report and urine toxicology testing at each quarterly visit, the second of which provided data for this assessment. Outcomes include sensitivity, specificity, positive- and negative predictive values (overall and stratified by age), sex-work setting, and HIV status.
Results: Among 200 women, prevalence of positive toxicology screening for ATS use was 14% (95% confidence interval [CI], 9.2, 18.9%) and concurrent prevalence of self-reported ATS was 15.5% (95% CI, 10.4, 20.6%). The sensitivity and specificity of self-reported ATS use compared to positive toxicology test results was 89.3% (25/28), and 96.5% (166/172), respectively. The positive predictive value of self-reported ATS use was 80.6% (25/31); the negative predictive value was 98.2% (166/169). Some differences in concordance between self-report and urine toxicology results were noted in analyses stratified by age group and sex-work setting but not by HIV status.
Conclusions: Results indicate a high prevalence of ATS use among FSW in Phnom Penh, Cambodia, and high concordance between self-reported and toxicology-test confirmed ATS use.
Financial Support: This study was financially supported by the research grants from the NIH (grants 1R21 DA025441 and 1R01NR010995).

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SUCCESS IN COCAINE TREATMENT TRIALS: WHICH DRUG USE OUTCOME IS MOST ASSOCIATED WITH CLINICAL IMPROVEMENT?

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Aims: There are a number of different strategies to measure success in cocaine dependence treatment trials. Some investigators evaluate cocaine use based on the number of cocaine-negative urine drug screens (UDS) provided by patients throughout the trial; some suggesting if at least 50% UDS are negative, it may indicate success (O'Brien & McLelland, 1996). Others measure the number of weeks of UDS verified cocaine abstinence; often defining success as achieving 3 weeks of continuous abstinence, typically at the end of the trial, or at any point during the trial (Kampman et al., 2002). Little is known about which cocaine use outcome is most closely associated with overall clinical improvement in cocaine dependent patients.
Methods: Data derived from 4 prior cocaine dependence pharmacotherapy trials (total N = 789) conducted at our Center were separated into 4 outcome groups: (1) cocaine-negative UDS ≥ 50%, but never 3 weeks clean, (2) 3 weeks clean at any point in the study, excluding the last 3 weeks, (3) last 3 weeks clean, and (4) patients not fitting in other groups. Groups were compared on improvement in scores of the Clinical Global Improvement (CGI), Hamilton Rating Scale for Depression (HAM-D), Addiction Severity Index (ASI) composites, and physical measures (i.e., weight, heart rate, blood pressure).
Results: There was a significant interaction between group and percentage of cocaine-negative UDS, with the highest percentage among patients in Group 3. Significant between-group differences existed for improvement in scores of the clinician-rated CGI, patient-rated CGI, HAM-D, and the ASI composite scores for drug, alcohol, and psychiatric problems, with greater improvement in Group 3. At follow-up, patients in Group 3 were significantly more likely to provide a cocaine-negative UDS than patients in other groups.
Conclusions: The outcome most closely associated with overall clinical improvement seems to be cocaine-negative UDS results during the last 3 weeks of a trial.
Financial Support: Supported by NIDA grant P50 DA12756

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THE MODIFYING EFFECTS OF REGULAR ALCOHOL USE ON PERCEIVED SOCIAL SUPPORT AND DEPRESSION IN ISRAEL.

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Aims: Previous research has consistently indicated that social support is associated with a reduced risk of depression. Few studies, however, have investigated how this relationship may be modified by alcohol use among populations affected by the perpetual threat of conflict, such as the case in Israel. This cross-sectional investigation explored the potentially modifying effects of regular alcohol use on the relationship between depression and perceived social support from family and friends among a nationally representative sample of Jewish and Palestinian Israelis in 2008.
Methods: Multivariable linear regression models were estimated to measure the associations of social support and depression. Interaction terms were then entered into the models to test for effect modification of social support and alcohol use.
Results: Results from 1622 Israeli participants indicated that increased social support from family was significantly associated with less depression symptomatology ($p<.0001$), however, this relationship was not significantly modified by alcohol use ($p=.17$). Social support from friends was also significantly associated with fewer depression symptoms ($p<.01$) but this relationship was significantly modified by alcohol use ($p=.015$). Stratified analyses revealed that although social support from friends was associated with fewer depression symptoms for both groups, the association was stronger for those who drank alcohol regularly ($n = 340$, $\beta=-1.27$, $p<.0001$) than for those who did not drink regularly ($n = 1282$, $\beta=-.44$, $p=.049$).
Conclusions: These findings may indicate that social support from friends is a more important protective factor for depression among regular drinkers than among non-regular drinkers in this context. Additional research is warranted to elucidate these relationships.
Financial Support: Mr. Kane is supported by the Drug Dependence Epidemiology Training Program (National Institute on Drug Abuse, T32DA007292).

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EXPANSION OF MEDICALLY ASSISTED TREATMENT (MAT) PROGRAMS IN MALAYSIA.

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Aims: To monitor evolving drug abuse problems and treatment programs in Malaysia, our research group has been conducting periodic epidemiological surveys evaluating untreated drug users and collecting and reviewing data on drug abuse treatment programs in Malaysia. In response to the continuing problems with heroin dependence and steadily increasing number of HIV/AIDS resulting from injection drug use, Malaysia introduced medically-assisted treatments (MAT) in early 2000s: Buprenorphine (BMT) in 2002; Methadone (MMT) in 2003. Currently there are ~380 general medical practice offices offering BMT for ~20,000 to 30,000 patients and 270 public or private MMT programs across the country with ~12,000 active patients. At the same time, there are 28 government drug rehabilitation centers with ~7,000 residents/inmates, and ~115 privately managed drug rehabilitation centers with ~ 2,000 residents. Recently, we observed a shift from heroin and morphine as the main problem drugs to ATS. In South East Asia, ATS ranks among the top 3 drugs and accounts for half of the world's methamphetamine users. Opiate users in Malaysia who are undergoing MMT or BMT frequently abuse ATS and treatments for co-occurring opiate and ATS dependent patients are urgently needed. The incidence rate of HIV appears to leveled off in the recent years with ~4000 new cases per year detected in 2009, 2010, and 2011 while ~6,000 per year were detected in the early 2000s
Conclusions: While changes observed in recent data on newly detected HIV cases cannot be directly linked to the introduction and expansion of MAT programs in Malaysia, implementation of MATs in early 2000s was followed by steadily increasing number of opiate dependent individuals receiving MAT treatments. New trends in drug use patterns underscore the need to develop and implement effective MAT treatments for co-occurring opiate and ATS and poly substance abuse disorders
Financial Support: USM Research University Grant (1001CDADAH816174), NIDA DA14718, CMHC/DMHAS/State of Connecticut

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SUBSTANCE ABUSE TREATMENT-SEEKING AND BARRIERS TO CARE IN PERSONS WITH ALCOHOL USE DISORDERS AND COMORBID MOOD OR ANXIETY DISORDERS.

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Aims: To compare the utilization of substance use disorder treatment services among individuals diagnosed with an alcohol use disorder (AUD) with and without a comorbid mood or anxiety disorder.
Methods: We used data from the National Epidemiologic Survey on Alcohol Related Conditions to examine perceived unmet need for substance use treatments and barriers to such care in 5,003 individuals with an AUD with a comorbid mood or anxiety disorder compared to 6,734 individuals with an AUD but without a mood or anxiety disorder. We hypothesized that the comorbid group would have greater use of services, but would also experience more barriers to care, than the non-comorbid group.
Results: Overall, the comorbid group was more likely to use substance treatment services than the non-comorbid group (18% vs. 12%, $p<0.001$). However, the comorbid group was also more likely to perceive an unmet need for such care (8% vs. 3%, $p<0.001$) and reported a larger mean number of barriers to care (2.81 vs. 2.20, $p=0.031$). Participants with comorbid disorders were more likely than those with non-comorbid AUD to experience financial barriers to care (19% vs. 10%, $p=0.032$).
Conclusions: Compared to individuals with AUD only, those with AUD and a comorbid mood or anxiety disorder experience a greater level of unmet need for substance use treatments and a larger number of barriers to such care, especially financial barriers. These individuals might benefit from expansion of financial access to mental health care and integration of services envisioned under the Affordable Care Act.
Financial Support: National Institute on Drug Abuse (DA030460-02 & T32DA007292) and National Institute on Alcohol Abuse and Alcoholism (AA016346).

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YOUTH IN FOSTER CARE USE DRUGS TOO: EXAMINING FACTORS THAT INFLUENCE FOSTER PARENT WILLINGNESS TO FOSTER SUBSTANCE-USING YOUTH.

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Aims: Youth in foster care are more likely than the general population to have an alcohol and other drugs (AOD) problem. There are no data examining the willingness of foster care parents to foster adolescents who use AOD. This study examines the willingness of a national sample of foster parents to foster AOD-using youth and examines drug, individual and agency-level factors that influence the decision.
Methods: Licensed foster parents (N=752, 86% female, M age=46.55) completed a 145-item nationally distributed online survey. Independent variables consisted of AOD-specific trainings attended, confidence in addressing the behaviors of AOD youth, confidence in having a positive effect on AOD youth, past helpfulness of placement agency in dealing with problem youth, and past difficulty attaining services for problem youth. Covariates included whether parents fostered a child with an AOD problem in the past, years as a foster parent, number of children typically fostered, religiosity, therapeutic foster parent status, and foster home type. The dependent variable was willingness to foster an AOD-using youth. Logistic regression analyses in SPSS were used.
Results: A slight majority of foster parent participants (61%) were willing to foster an AOD-using youth but willingness decreased by type of drug used (e.g., 18% for designer drugs). Attending AOD trainings was a significant predictor of willingness to foster ($b=.38$, $p<.05$), however, this effect was mediated by parental confidence in dealing with AOD behaviors ($b=.87$, $p<.001$) and in having a positive effect on youth ($b=.31$, $p<.05$). Parents who reported that their foster care agency was not helpful were significantly less willing to foster ($b=-.60$, $p<.05$).
Conclusions: These findings shed light on barriers that impede parent willingness to foster AOD-using foster care youth. At an individual level, providing foster parents with skill-based training that increases confidence is needed. At a systems level, increasing placement agency responsiveness, foster care slots, other fostering models, and AOD training is indicated.
Financial Support: NIDA Grant #P50-DA027841

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DIFFERENCES IN PREVALENCE OF HIV AND HCV BETWEEN BLACKS AND WHITES BASED ON PATTERNS OF INJECTION AND NON-INJECTION DRUG USERS IN BALTIMORE CITY.

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Aims: The current study examined differences in the prevalence of viral hepatitis C and HIV disease between Blacks and Whites adults in Baltimore City across three subtypes of drug users identified in previous research (Harrell et al, 2012): crack/nasal heroin users, heroin injectors, and polysubstance users.
Methods: This study was a part of an ongoing NIDA-funded NEURO-HIV Epidemiologic study, a longitudinal study to identify neuropsychological and social-behavioral HIV risk factors among injection and non-injection drug users.
Results: The subsample of 482 participants included 284 men (58.9%) and 198 women (41.1%). Approximately half of the participants self-identified as White (n = 244), while the rest self-identified as Black (n = 238). There were significant differences between classes based on race (X2 (2, N = 482) = 97.84, p = .00) and HCV (X2 (2, N = 482) = 140.87, p = .00). Differences indicated that crack/nasal heroin users were predominantly Black (74.9%), while heroin injectors and polysubstance users were predominantly white (71.5% and 68.9%). Polysubstance users accounted for over half of the HCV positive diagnoses (56.5%) in Whites. Blacks HCV diagnoses were somewhat evenly spread across the groups. Though HIV did not differ significantly between groups, the Crack/Nasal Heroin contained over half (52.4%) of the 42 HIV positive diagnoses in the sample.
Conclusions: Black drug users in this sample were characterized by significantly lower rates of IDU compared to whites. Since the vast majority of the current sample is heterosexual, the findings suggest heterosexual sex as the primary mode of HIV transmission for Black drug users. In contrast, White drug users were more prone to HCV compared to Black drug users, which is attributable to their higher rate of IDU. The current study findings provide further support that heterosexual transmission of HIV is a primary vector of disease transmission among African American drug users who predominantly do not inject drugs and thereby may help to inform targets of disease prevention.
Financial Support: NIDA: RO1 DA 14498

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VALIDITY OF A BRIEF SCREENER FOR ADOLESCENT TOBACCO, ALCOHOL, AND DRUG USE.

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Aims: To determine the initial validity of a new brief screening measure in a sample of adolescent pediatric patients.
Methods: Adolescents ages 12-17 (*N*=381) waiting for primary care appointments at 1 of 3 sites of a federally qualified health center in Baltimore were recruited for a study evaluating a new measure for screening and assessing substance use. Participants completed NIAAA's alcohol screener about their drinking in the past 12 months. For the current study, NIAAA's screener was expanded to also ask about tobacco and drug use. Our Brief Screener for Tobacco, Alcohol, and Drugs (BSTAD) was concurrently administered with the CIDI, CRAFFT, and ASSIST. We examined the agreement of the BSTAD with the lead-in screening questions in the CIDI (covering past 12–month use), the CRAFFT (past 12-month use), and the ASSIST (lifetime use). Receiver operating characteristic (ROC) curves and kappa values were used to examine agreement between the BSTAD and CIDI, CRAFFT, and ASSIST, and to estimate the sensitivity and specificity of the BSTAD relative to the 3 screening tools in predicting use of any substance.
Results: ROC analyses indicated extremely high concordance between the BSTAD and the CIDI (Area Under the Curve = .95 [*SE*=.02]) and CRAFFT (.93 [.02]), and less so with the ASSIST (.78 [.02]). Sensitivities of the BSTAD with the CIDI (.91 [.03]) and CRAFFT (.89 [.03]) were quite high, in contrast to the ASSIST (.55 [.04]). Specificities of the BSTAD with the CIDI (.99 [.01]), CRAFFT (.97 [.01]), and ASSIST (1.0) were all quite high. Likewise, kappa showed very high agreement between the BSTAD and the CIDI (.91 [.02]) and CRAFFT (.87 [.03]), and lower agreement with the ASSIST (.54 [.04]).
Conclusions: Findings suggest a high degree of agreement between the BSTAD and the screening questions in the CIDI, CRAFFT, and ASSIST. The likely explanation for the lower sensitivity and kappa values with the ASSIST is that it screened for lifetime use rather than past 12-month use as screened for in the BSTAD, CIDI, and CRAFFT.
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DAYSIMETER FEASIBILITY AND ACCEPTABILITY IN A POLYSUBSTANCE-USING POPULATION.

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Aims: Cocaine use could reduce sensitivity to blue light and thereby disrupt circadian rhythms. In this study, we evaluated circadian entrainment in cocaine users by having them wear the Daysimeter, a device that measures activity and eye-level visible- and circadian-light exposures in the field. The main goal was to evaluate the acceptability of the Daysimeter in this population, but we also hypothesized that greater levels of circadian disruption would be associated with greater drug use.
Methods: Fifteen methadone-maintained heroin and cocaine users (11 men, 4 women) wore the Daysimeter for two three-day intervals (Mon-Wed and Fri-Sun) and reported drug use in real time on electronic diaries. Participants also rated the Daysimeter's physical comfort and social acceptability at the end of each wearing period. Circadian entrainment was assessed by phasor analysis: phasor magnitudes reflect the degree to which activity data correlate with circadian light exposures; phasor angles reflect the activity-light offset (i.e., whether activity is more nocturnal or diurnal). Phasor analyses were done separately for weekends and weekdays. Phasor magnitudes were compared with drug-use indices (electronic-diary data and thrice-weekly urine) in multilevel models. Acceptability surveys were summarized in terms of *a priori* cut points.
Results: Four of the 11 participants' Daysimeter data could not be analyzed due to partial noncompliance. However, all 15 participants rated the usage of the Daysimeter as easy/very easy, with few reporting physical or social discomfort. Phasor magnitude and angle were not associated with current cocaine and/or opiate use and (unlike in other populations) did not differ between weekdays and weekends.
Conclusions: The Daysimeter is feasible to use in polydrug-using outpatients. However, their circadian entrainment was not acutely associated with drug use.
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TAXOMETRIC ANALYSIS OF DSM-IV AND DSM-5 ALCOHOL USE DISORDERS.

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Aims: The purpose of this study was to investigate the latent structure of DSM-Fourth Edition (DSM-IV) and proposed DSM-5 alcohol use disorders.
Methods: The study used the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) to conduct taxometric analyses of DSM-IV and DSM-5 alcohol use disorders defined by different thresholds to determine the taxonic or dimensional structure underlying the disorders.
Results: DSM-IV and DSM-5 abuse and dependence indicators associated with 3+ and 4+ thresholds met validity standards (< 1.2 SD). As required nuisance covariance was moderate to high in the total samples but low within the taxon and complement groups. A priori taxon base rates were 0.110 and 0.068 for the 3+ and 4+ thresholds. Corresponding base rates for DSM-5 criteria were similar, 0.117 and 0.073. DSM-IV and DSM-5 alcohol abuse and dependence criteria with 3+ thresholds demonstrated dimensional structure, with CCFI estimates of 0.338 and 0.332. Corresponding thresholds with 4+ criteria were taxonic, as were thresholds defined by cut-offs of 5+ and 6+ criteria, with CCFI estimates of 0.763 and 0.735.
Conclusions: DSM-IV and DSM-5 alcohol use disorders demonstrated a hybrid taxonic-dimensional structure. That is, DSM-IV and DSM-5 alcohol use disorders may be taxonically distinct compared to no disorder if defined by a threshold of 4 or more criteria. However, there may be dimensional variation remaining among non-problematic to subclinical cases. A systematic program of structural research using taxometric and psychometric procedures is warranted.
Financial Support: The National Institute on Alcohol Abuse and Alcoholism (NIAAA) funded the survey. Support acknowledged for Mr. Kerridge, NIH/NIDA Fellowship F31DA025377. Received funding from the European Community's Seventh Framework Programme (FP7/2007-2013), under Grant Agreement no 266813 - Addictions and Lifestyle in Contemporary Europe - Reframing Addictions Project (ALICE RAP).

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THE IMPACT OF GENETIC PREDICTORS OF DRUG DEPENDENCE ON NEUROIMMUNE AND ENDOCRINE MARKERS.

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Aims: Genetic polymorphisms in the innate immune and neurological pathways have been associated with an increased risk of drug dependence. However, the functional consequences of these variations on the physiological and psychological responses to addictive drugs remain unclear. Of particular interest is the stress response, mediated through the hypothalamic-pituitary-adrenal (HPA) axis and influencing immune function. The combination of the G allele at -511 and the A allele at -31 in the *interleukin(IL)-1β* gene has been associated with an increased risk of developing opioid dependence. This study aims to assess whether *IL-1β* genetic variation influences peripheral stress markers in response to the administration of oxycodone.
Methods: Healthy Caucasian volunteers (n=25) were administered a single oral dose of immediate release oxycodone hydrochloride (Endone, 20mg). At 0, 1, 2, 4 and 6 hours post-administration, blood and saliva samples were collected along with assessment of pupil diameter. The results were compared to genotype at the -511 and -31 positions in the *IL-1β* gene.
Results: Cortisol levels two hours post-administration were significantly higher in the heterozygous (-511 G/A, -31 G/A) population than the homozygous (-511 G/G, -31 A/A) population ($p<0.05$). Pupil diameter, a surrogate measure of plasma drug concentration, was not significantly different between the homozygous and heterozygous populations at each time point.
Conclusions: Individuals genetically predisposed to dependence exhibit an altered stress response to administration of an opioid drug, possibly due to a lack of HPA axis activation. These subjects may be more likely to self administer drugs when coping with stressful situations. These results will be compared with a non-drug control group.
Financial Support: This research was supported by an Australian Postgraduate Award

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DIFFERENTIAL COGNITIVE IMPAIRMENTS INDUCED BY METHAMPHETAMINE AND/OR HIV GP120 EXPRESSION IN THE MOUSE.

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Aims: Methamphetamine (METH) abuse is common among HIV-infected individuals. However, the effects of METH on cognitive function in HIV patients are not known. We investigated the separate and combined effects of a METH binge and the expression of the HIV gp120 protein on cognitive function in adult male transgenic (gp120TG) and control mice.
Methods: Mice were exposed to an escalating METH regimen followed by a METH binge, and tested in a battery of cognitive tasks including the novel object/location recognition, the Barnes maze, the attentional set-shifting task (ASST) and the social preference/recognition tests.
Results: Gp120 expression led to deficits in discrimination learning in the ASST and deficits in reversal learning in the Barnes maze test indicating deficits in both learning and executive function. METH exposure tended to impair novel object recognition and led to impaired spatial strategy in the Barnes maze test indicating deficits in recognition memory and spatial learning. Mice expressing gp120 and treated with METH had lower spatial strategy scores than all other groups on the final acquisition trials in the Barnes maze test, suggesting that the progression from a serial to a spatial search strategy was impaired. Interestingly, METH exposure tended to improve gp120-induced deficits in discrimination learning while leading to a decline in discrimination learning in control mice. Social preference/recognition and novel location recognition was similar in all mice.
Conclusions: Although HIV infection involves the interactions of multiple proteins/processes in addition to gp120, our findings in gp120TG mice suggest that humans with the dual insult of HIV infection and METH abuse may exhibit a broader spectrum of cognitive deficits due to the cumulative effects of each factor. However, depending on the cognitive domain, the combination of both insults may lead to further deficits in cognition or, alternatively, improvements in aspects of cognitive performance.
Financial Support: Translational Methamphetamine AIDS Research Center NIDA grant P50 DA26306

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ALCOHOL AND PSYCOACTIVE SUBSTANCES ABUSE IN BRAZIL: A CROSS-SECTIONAL STUDY.

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Aims: The objective of the present study was to describe and measure patterns of alcohol and drug use in five regions of Brazil, representative of the urban Brazilian population where there are specific programs to minimize the violence and criminality.
Methods: By means of a cross sectional study including a sample of patients of all institutions located in the five studied areas registered at the Nacional Secretary of Alcohol and Drugs (SENAD) that provide health assistance to the people who abuse alcohol and/or other psychoactive substances. The study was performed between November 2011 and March 2012. Demographic characteristics were collected and the abuse of alcohol and psychoactive drugs was assessed through the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST).
Results: The studied sample included 1649 individuals. Males were predominant (60%). The mean age was 39.8±13.8. Alcohol was the most frequently used substance reported corresponding to 31% in the whole sample and, varying from 17% to 59%, according to the region. Cocaine was reported by 19%, tobacco, crack, and marijuana from 18%, 17%, and 14%, respectively. About 94% informed had never used injected drugs.
Conclusions: In Brazil, the abuse of alcohol and of psychoactive substances among those who seek help is elevated, whereas injected drug use seems to be rare.
Financial Support: Grant from the National Secretary of Alcohol and Drugs (SENAD), Brazil

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SLEEP QUALITY AMONG CANNABIS USERS SEEKING TREATMENT.

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Aims: Sleep is important for human well-being. Most daily cannabis users report sleep difficulty during abstinence, and often report sleep problems contribute to relapse. The present study is being conducted to evaluate the quality of sleep among cannabis users seeking treatment.
Methods: Participants seeking treatment for a cannabis use disorder completed the self-report Pittsburgh Sleep Quality Index (PSQI), and those eligible for participation in an ongoing clinical trial then complete an overnight sleep assessment during which sleep was objectively measured via activity and EEG devices.
Results: Subjective reports from the first 12 participants indicate an average sleep latency of 39 minutes and a total sleep time of only 5.4 hours each night. Average (SD) global PSQI score for the sample was 17 (10), and the global PSQI score was >5, indicative of poor sleep, for 10 of 12 participants. Objective sleep assessments indicated frequent nocturnal awakenings, totaling an average of 69 minutes of time awake per night.
Conclusions: Most participants presenting for cannabis treatment in this trial have disordered sleep at intake, and abrupt cannabis cessation further deteriorates sleep continuity and architecture. Incorporation of clinical interventions aimed at improving sleep may be crucial for aiding initial and long-term abstinence rates in this subpopulation of cannabis users.
Financial Support: NIDA grant U01-DA031784

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PRESCRIPTION OPIOID USE AND RISK OF CARDIOVASCULAR DISEASE AMONG OLDER ADULTS FROM A COMMUNITY SAMPLE.

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Aims: Prescription opioid use has grown exponentially in the US over the last decade. Controversy exists about whether opioid use increases the risk of cardiovascular disease (CVD). We examined the association of prescription opioid use with coronary heart disease (CHD) and CVD mortality among community-dwelling adults, controlling for CVD risk factors and chronic pain.
Methods: Prescription opioid use was examined in 29,670 participants of the REasons for Geographic and Racial Differences in Stroke (REGARDS) study, a national cohort of black and white adults aged ≥ 45 years and recruited between 2003-7. Participants answered survey questions about medical history and behaviors, and physiologic measures and medications were assessed through pill bottle review in the home. Telephone follow-up was conducted every 6 months and CHD events and cause of death were expert adjudicated. Sequentially adjusted Cox proportional hazards models examined associations of opioid use with CHD events and CVD death. Covariates included socio-demographics, CVD risk factors, depressive symptoms and chronic pain.
Results: The study sample had mean age 64.9±9.4 years, with 41.1% blacks and 55.1% women. Median follow up was 4.4 years and there were 1171 CHD events and 939 CVD deaths. Among the 7.6 % (n=2,265) of participants who reported prescription opioid use (POU) at baseline, 10.7% (n=247) used >2 opioid medications simultaneously, 5.7% (n=132) had no prescription. POU included more women, smokers, and persons with lower SES and higher levels of depressive symptoms. 118 CHD events and 107 CVD deaths occurred among opioid users. The adjusted hazard ratio (HR [95% CI]) for POU associated with CHD events was 1.26 [1.01-1.57], which lessened to 1.18 [0.95-1.49] with the addition of chronic pain. The adjusted HR associated with CVD death was 1.33 [1.05-1.70], even after adjustment for chronic pain.
Conclusions: Prescription opioid use among older adults from this community sample was associated with CVD mortality even after adjusting for a host of baseline CVD risk factors.
Financial Support: NHLBI RO1HL080477

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THE ROLE OF ALPHA3BETA4 NICOTINIC RECEPTORS IN COCAINE-INDUCED REWARD ACQUISITION AND BEHAVIORAL SENSITIZATION.

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Aims: Recent studies suggest a role for the alpha3beta4 neuronal nicotinic acetylcholine receptor (nAChR) subtype in drug-seeking behavior. Alpha3beta4 nAChRs are located in the medial habenula and interpeduncular nucleus, regions that have been implicated in the regulation of ventral tegmental area dopaminergic neurons. Previously, the non-selective, modest affinity alpha3beta4 nAChR antagonist 18-methoxycoronaridine has been shown to reduce drug self-administration and attenuate cocaine conditioned place preference (CPP). We recently showed that a highly selective alpha3beta4 nAChR antagonist AT-1001 potently inhibits nicotine self-administration in rats. In this study we further examined whether AT-1001 and a novel highly selective alpha3beta4 antagonist, AT-1012, could alter cocaine-mediated behaviors in mice. Both AT-1001 and AT-1012 have nanomolar affinity for the alpha3beta4 nAChR subtype and over 100-fold selectivity versus other nAChR subtypes.
Methods: The CPP paradigm was used to examine whether AT-1001 and AT-1012 would alter reward acquisition and behavioral effects of cocaine.
Results: AT-1001 and AT-1012, when given alone did not produce CPP or conditioned place aversion. When given as a pretreatment to 5 mg/kg cocaine, both AT-1001 (1-10 mg/kg) and AT-1012 (3-10 mg/kg) blocked cocaine CPP. AT-1001 (1-3 mg/kg) did not alter cocaine-induced global activity, whereas 10 mg/kg AT-1001 suppressed global activity. At the higher dose of cocaine (30 mg/kg), AT-1001 (1-3 mg/kg) did not block cocaine CPP but blocked cocaine-induced behavioral sensitization to global activity, a behavioral effect observed at 30 mg/kg and not 5 mg/kg dose of cocaine.
Conclusions: These studies indicate that AT-1001 and AT-1012 can attenuate various facets of the cocaine reward process such as acquisition of reward and behavioral sensitization, and suggest that the alpha3beta4 nAChR may be a good target for further medication development for treatment of psychostimulant drug addiction.
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A RANDOMIZED TRIAL OF INTEGRATED CARE FOR METHADONE-MAINTENANCE PATIENTS WITH CO-OCCURRING PSYCHIATRIC DISORDERS.

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Aims: Integrating psychiatric treatment services within substance abuse treatment settings is a promising service delivery model, but has not been evaluated using random assignment to psychiatric treatment setting and controlled delivery of psychiatric care. This study evaluates the efficacy of integrated service delivery in an opioid-agonist treatment program on psychiatric and substance use outcomes.
Methods: Opioid abusers with at least one co-occurring psychiatric disorder were randomly assigned to Integrated Substance Abuse and Psychiatric Care (ISAP: n=160) or Parallel Substance Abuse and Psychiatric Care (PSAP: n=156), and observed for one-year. All participants received methadone maintenance at the substance abuse program. ISAP participants received all psychiatric care at the substance abuse program; PSAP participants received a similar scope and frequency of psychiatric services at a community psychiatry program on the same campus. Psychiatric care included psychiatrist appointments, individual and group therapy sessions, and good access to psychiatric medications. Primary outcomes included psychiatric service utilization and retention, changes in psychiatric distress (using the SCL-90-R Global Severity Index-GSI), and urinalysis results.
Results: ISAP participants were more likely to initiate psychiatric care (97% vs. 79%, $p < .001$), remained in psychiatric treatment longer (M = 196 vs. 102 days; $p < .001$), utilized more psychiatric services (M = 24 vs. 15 sessions; $p < .001$), and enjoyed greater reductions in psychiatric distress (Difference in GSI change scores = 2.80; $p = .002$) than PSAP participants. No differences were observed for drug use outcomes.
Conclusions: Integrated psychiatric and substance abuse care in a community opioid agonist setting improved psychiatric, but not substance abuse, outcomes. These findings provide evidence to support the efficacy of integrated care for opioid abusers, demonstrate limitations of this treatment model, and suggest clinical research opportunities for improving outcomes for more participants.
Financial Support: NIDA grant R01DA016375

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IMPACT OF A 12-STEP FACILITATION INTERVENTION ON TOBACCO SMOKING OUTCOMES IN COMMUNITY TREATMENT PROGRAMS.

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Aims: The present study is a secondary analysis (N=258) exploring tobacco smoking status and nicotine dependence in stimulant dependent patients enrolled in a large NIDA Clinical Trials Network (CTN) multisite study investigating the impact of 12 Step Facilitation integrated with treatment as usual (TAU) versus TAU alone on stimulant use outcomes.
Methods: The Self Report Substance Use Calendar (SUC) and the Fagerstrom Test for Nicotine Dependence (FTND) were obtained at baseline, 8 weeks, 3 and 6 months follow-up. We fit generalized estimating equations (GEE) to estimate the effects of treatment group assignment on FTND scores over follow-up. Smoking status and self-report stimulant abstinence were compared at post treatment and follow-up using Chi – Square analysis.
Results: Eighty-one percent participants endorsed smoking at baseline. The average FTND score at baseline was 4.38 + 2.14. Controlling for baseline FTND score, we observed a small but significant reduction in FTND scores over time in the 12-step group ($\beta = -0.35$, FTND score range 0-10; $p=0.04$) with a trend at week 8 ($p = 0.06$), and non-significant reductions at months 3 and 6. At both 8 weeks and 3 month follow-up smoking status (yes/no) did not differentially affect stimulant use. However, at 6 months, 85.7% of nonsmokers and 67.7% smokers reported past 30 day stimulant abstinence ($X2 = 10.062$, $p < 0.002$).
Conclusions: The 12 Step Facilitation intervention had a modest impact on nicotine dependence scores. Continued smoking post-treatment is associated with stimulant relapse.
Financial Support: NIDA Clinical Trials Network U10 DA13727 (Brady PI), U10DA13714 (Donovan, PI)

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GENDER MODIFYING EFFECTS ON THE ASSOCIATION BETWEEN STRESS AND CRAVING.

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Aims: Given the proposed addition of craving in the DSM-5, further research on the mechanisms driving craving is warranted. This study explores the relationship between the number and type of past-year stressful life experiences (SLEs) and past-year alcohol craving. We also assess whether gender modifies this relationship.
Methods: Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 2, years 2004-2006 who were past-year drinkers (n=22,152). Factor analyses grouped the 14 SLEs assessed in Wave 2 into four separate types: proximal, financial, victimization, and corollary stressors. Craving was measured by mild and severe indicators. Weighted multinomial logistic regressions examined how SLE types predicted mild and severe) craving. Analyses were adjusted for age, sex, race/ethnicity, education, and past-year mood/anxiety disorders. Interactions between gender and SLE type were also tested.
Results: Females had a higher mean number of past-year SLE experiences than males (1.42 vs 1.38), and had higher rates of experiencing all SLE types except victimization. In the adjusted models, all four SLE types increased the odds of endorsing severe craving, with OR ranging from 1.9 [1.2, 3.0] for victimization to 2.8 [1.9, 4.3] for proximal stressors. Significant interactions were found between gender and each SLE type.The OR for males experiencing financial stress compared to males without stress was higher than the same relationship for females (2.5[1.4-4.4] vs 2.2[1.2, 4.2], while the OR for males experiencing corollary stressors compared to males without the stress was lower than the same relationship for females (2.2[1.4, 3.6] vs 2.6[1.4, 4.9]). Statistically significant interactions were found consistently across all SLE types, indicating higher odds of craving among males compared to females after experiencing the same type of stressor.
Conclusions: The effect of SLEs on the subjective experience of craving appears to vary by gender and stress type. This may reflect differential coping mechanism by gender.
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REINFORCING ATTENDANCE TO INTEGRATED PSYCHIATRIC TREATMENT: EFFECTS ON PSYCHIATRIC DISTRESS.

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Aims: The high prevalence of psychiatric disorders in patients with substance use disorder, coupled with low rates of psychiatric service utilization in this population, has encouraged development of integrated care treatment models. The present study examines the efficacy of contingency management for improving adherence and response to psychiatric services integrated on-site at a community-based opioid agonist program.
Methods: Methadone maintenance outpatients with at least one current SCID-IV psychiatric disorder were randomly assigned to: 1) reinforced on-site integrated care (ROIC), with vouchers (worth $25.00) contingent on full adherence to each week of scheduled psychiatric services; or 2) standard on-site integrated care (SOIC). All participants received access to the same schedule of twice monthly psychiatrist and weekly individual and group mental health counseling sessions for 12-weeks. All participants received similar schedules of stepped-care substance abuse treatment services. The Global Severity Index (GSI) of the Symptom Checklist-90-R (administered at baseline and weeks 4, 8, 12) evaluated changes in psychiatric distress.
Results: Preliminary analyses show that ROIC participants (n=40) had reductions in GSI severity from baseline (M=51) to the mean of the three follow-up scores (M=45; $p < .001$); SOIC participants (n=40) had similar baseline (M=49) and follow-up (M=48) scores (p=.078). Comparison of these change scores was not significant (p = .147). Multiple regression analysis showed that across conditions the number of individual and group counseling sessions attended was associated with reduction in reported distress (p=.05).
Conclusions: Preliminary results suggest that reinforcing adherence to psychiatric services improves response to an on-site integrated model of psychiatric care. Analysis of the full study sample (n=125) will provide greater statistical power to detect between group differences in change scores and to test relationships between distress reduction and substance use.
Financial Support: NIDA DA028154-02

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EFFICACY OF CRAFT WHEN MODIFIED FOR PARENTS OF TREATMENT-RESISTANT ADOLESCENTS: PRELIMINARY RESULTS.

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Aims: Little research has examined methods for helping a parent with a treatment-resistant child. We adapted the Community Reinforcement and Family Training (CRAFT) program for treatment-resistant adults for use by parents dealing with a treatment resistant child (12-25 yrs old) and evaluated the revised program on acceptability to parents and efficacy in facilitating treatment entry of the child.
Methods: The revision of the CRAFT program was informed by a review of the behavioral parent training literature and by consultation with adolescent treatment and CRAFT experts. This resulted in the addition of two modules: behavior monitoring and behavior-reducing consequences. Parents (N=22) were randomly assigned to receive 12 individual sessions of either modified CRAFT (n = 12) or Alanon/NarAnon Facilitation Training (AFT; n = 10) delivered at our Family Training Program (FTP). Parents' treatment attendance and child treatment entry was monitored weekly and at 4- and 6- month follow-up assessments.
Results: Treatment acceptance was good in both groups, with 100% retention of parents in CRAFT and 90% retention in ANF. Large differences were seen in the number of children receiving a treatment referral with 67% of the CRAFT parents getting their child to FTP for a referral compared to 10% in the ANF group. Rates of transferring youth from FTP to specialty treatment in the community was much lower: 33% vs 20% in CRAFT and ANF, respectively.
Conclusions: Preliminary results suggest that the modified CRAFT program is acceptable to parents and is more efficacious than ANF in getting the child to the family program; however, as in similar studies examining referral of substance-using individuals to specialty treatment, rates of successful transfer from one program to another is very low. This work suggests that youth treatment rates might be improved by providing parent and child services at the same site.
Financial Support: P50 DA027841

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ORGANIZATIONAL DYNAMICS, LEARNING ENVIRONMENTS, AND INTEGRATION OF TECHNOLOGY IN SUBSTANCE ABUSE TREATMENT.

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Aims: Prior research demonstrates that organizational factors influence the implementation of innovations including technological advances and electronic health records (EHR). Preliminary evidence has also demonstrated the potential for such tools to enhance the quality of care, efficiency of service delivery, and organizational decision-making capacities consistent with a learning organization. This study examines the relationship between technology integration and organizational factors that support or impede the use of technology in substance abuse treatment centers.
Methods: A longitudinal qualitative study was conducted using semi-structured interviews and focus groups from 2009-2011. Participants were clinical supervisors, agency directors, and financial administrators. Phase I consisted of 107 participants (59% female) and Phase II consisted of 56 participants (55% female). The research team used an iterative process to identify code schemes within the data (Phase I IRR = 75%; Phase II IRR = 88%). Atlas.ti software was used to analyze codes regarding technology and organization.
Results: Data suggest that technology is utilized as a tool to facilitate treatment interventions, staff training, communication, and utilization of electronic records. Analysis within each of these core domains revealed organizational factors that correspond with the integration of technology. The factors include management of health records, fidelity monitoring, and internal communication. A consistent pattern of acceptance and increased incorporation of technology was also evident over time.
Conclusions: Data indicate a slow but successful integration and acceptance of technology in addiction clinics. These findings also point to the core organizational domains that appear to support the use of technology (management of health records, fidelity monitoring, and internal communication). These factors may create a learning environment that is supportive of the adoption of both technology and other innovative practices.
Financial Support: This work was supported by the NIDA Career Development Award K23 DA021225

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PSYCHOSOCIAL INTERVENTIONS TO REDUCE ALCOHOL CONSUMPTION IN CONCURRENT PROBLEM ALCOHOL AND ILLICIT DRUG USERS: COCHRANE REVIEW.

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Aims: To assess the effects of psychosocial interventions for problem alcohol use in illicit drug users (principally problem drug users of opiates and stimulants)
Methods: This systematic review of randomised controlled trials included adult illicit drug users with concurrent problem alcohol use.
We searched the following databases (November 2011): Cochrane Library, PUBMED, EMBASE, CINAHL, PsycINFO and reference list of articles. We also searched conference proceedings and online registers of clinical trials. Two reviewers independently assessed risk of bias and extracted data from included trials.
Results: Four studies, 594 participants, were included. Half of the trials were rated as having high or unclear risk of bias. The four studies considered six different psychosocial interventions grouped into four comparisons: (1) cognitive-behavioural coping skills training versus 12-step facilitation (N = 41), (2) brief intervention versus treatment as usual (N = 110), (3) hepatitis health promotion versus motivational interviewing (N = 256), and (4) brief motivational intervention versus assessment-only group (N = 187). Differences between studies precluded any pooling of data. Findings are described for each trial individually. Most findings were not statistically significant except for comparison 2: decreased alcohol use at three months (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.19 to 0.54) and nine months (RR 0.16; 95% CI 0.08 to 0.33) in the treatment-as-usual group; comparison 4: reduced alcohol use in the brief motivational intervention (RR 1.67; 95% CI 1.08 to 2.60).
Conclusions: No conclusion can be made because of the paucity of the data and the low quality of the retrieved studies.
Financial Support: The work on this review and poster was funded by a Cochrane Fellowship from HRB Ireland (CTF-2010-09), and a NIDA INVEST Drug Abuse Research Fellowship.

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ACTIVATION OF G-PROTEIN AND C-JUN N-TERMINAL KINASE BY KAPPA OPIOID RECEPTOR LIGANDS.

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Aims: The functional activity of a ligand depends on its ability to bind a receptor and elicit a signal to downstream effectors. The purpose of this study was to compare the activity of several kappa opioids, full agonists and partial agonists, by measuring G-protein and c-Jun N-terminal kinase (JNK) activation.
Methods: G-protein activation was measured using the [^{35}S]GTPγS binding assay in membranes prepared from Chinese hamster ovary (CHO) cells stably transfected with the human kappa opioid receptor (hKOR). Activation of JNK was determined using ELISAs to measure changes in total JNK and phosphorylated JNK (pJNK) in hKOR-CHO cells. Concentration-response curves were determined for both assays.
Results: U50,488 was a full kappa agonist in both the [^{35}S]GTPγS and pJNK assays with E_{max} values of 140% and 120%, respectively. None of the compounds tested altered total JNK levels. U50,488 was 8-fold more potent in the pJNK assay than the [^{35}S]GTPγS assay. Nalmefene was a partial agonist in both assays producing 50% stimulation in the [^{35}S]GTPγS assay and 37% stimulation in the pJNK assay. Nalmefene was equipotent in both assays. Nalmefene partially inhibited U50,488-induced stimulation of [^{35}S]GTPγS binding (I_{max} = 51%, IC_{50} = 9.2 nM) and pJNK levels (I_{max} = 62%, IC_{50} = 3.9 nM). Other kappa receptor ligands, nonselective and selective, including naltrexone, buprenorphine, and endogenous opioid peptides were tested in both assays.
Conclusions: The results indicate a similarity in the functional profiles of these kappa ligands at the proximal level of the G-protein and the more downstream JNK. Additionally, the greater potency of some ligands in the JNK assay may suggest activation of additional signaling pathways leading to the activation of JNK. Further research on the effects of opioid ligands on various downstream effectors will be beneficial to understanding the pathways involved in the physiological effects of opioids and toward medications development.
Financial Support: Paul Stark Endowed Professorship and the Margo Cleveland Fund.

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THE EFFECTIVENESS OF THE TREATMENT RETENTION AND INDUCTION PROGRAM (TRIP) FOR IMPROVING ADOLESCENT DECISION-MAKING.

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Aims: Substance abuse treatment should promote development of good judgment and decision-making, emphasizing thoughtful planning and drug-resistance in social settings. The purpose of this study is to examine the effectiveness of TRIP, a manualized intervention that uses a graphic approach—Mapping Enhanced Counseling—to promote systematic thinking among adolescents in treatment. Also of interest is the degree to which clients with attention issues benefit from TRIP.
Methods: Data were collected in 2011 and 2012, as part of the TCU Adolescent Project and represent 506 adolescents from 6 residential programs that completed assessments at intake and at 35 days (Time 2). Half of the sample (n = 251) enrolled in treatment prior to implementation of TRIP (Standard Practice Group); 255 clients entered treatment after TRIP implementation began and received Standard enhanced by TRIP. ANCOVAs were used to examine Time 2 differences by TRIP, Gender, and Attention groups, controlling for demographic and judgment measures at Time 1.
Results: Compared to Standard Practice, adolescents receiving TRIP scored higher on Decision-Making (DM), even after controlling for Gender, Drug use Severity, Age, Juvenile Justice Involvement, Attention, and DM at Time 1. Premeditation (thinking before acting) was marginally higher among TRIP clients without attention difficulties. Perceived control over drug use decisions was lower in the TRIP group (among all males and among females without attention difficulties), suggesting greater personal insight into their ability to resist drug use in social situations.
Conclusions: Findings suggest that TRIP promotes positive judgment and decision-making among adolescents, and that effectiveness varies by background characteristics such as gender and attention difficulties. Future studies should examine which specific elements of TRIP are most relevant for improving decision-making and test explanatory models of how changes in judgment and decision-making affect treatment motivation, retention, and engagement.
Financial Support: NIDA R01DA013093.

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HIV/AIDS SERVICES IN SUBSTANCE USE DISORDER TREATMENT PROGRAMS WITHIN THE CLINICAL TRIALS NETWORK.

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Aims: Previous research on HIV/AIDS-related services in substance use disorder (SUD) treatment has generally focused on the availability of HIV testing with less consideration of other prevention and supportive services. This study examines the adoption of HIV/AIDS-related services in treatment programs affiliated with NIDA's Clinical Trials Network (CTN), with comparisons between opioid treatment programs (OTPs) and SUD treatment programs.
Methods: Face-to-face interviews were conducted in 2011-2012 with administrators and clinical directors of 167 treatment programs that were members of NIDA's CTN (response rate = 79.9%). Dichotomous indicators measured whether programs: (1) conducted HIV risk assessments at treatment intake; (2) offered HIV education/prevention; (3) had adopted on-site HIV testing; (4) offered support groups for people with HIV/AIDS; and (5) provided on-site medical monitoring for people with HIV/AIDS (e.g., monitoring HAART compliance).
Results: HIV risk assessment (86.2%) and HIV prevention/education (79.1%) were widely adopted by treatment programs in the CTN. About 54.7% of programs offered on-site HIV testing, consisting of 30.8% of programs using rapid HIV tests and another 23.9% using non-rapid tests. Fewer programs provided HIV support groups (22.9%) and medical monitoring for people with HIV/AIDS (24.8%). Opioid treatment programs were more likely than other SUD programs to offer on-site HIV testing (79.2% vs. 50.4%, $p<.01$) and support groups for people with HIV/AIDS (41.7% vs. 19.6%, $p<.05$).
Conclusions: Although most treatment programs assess risk behaviors and offer HIV prevention/education, only half of the treatment programs within the NIDA CTN provide on-site HIV testing, which is a critical strategy for ensuring that patients receive their test results. Testing services have become widespread, however, within opioid treatment programs, which may reflect heightened concerns regarding the transmission of HIV/AIDS through injection drug use for their patient population.
Financial Support: Supported by the National Institute on Drug Abuse (R01DA14482).

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LONG-LASTING SENSITIZATION INDUCED BY A SINGLE EXPOSURE TO MORPHINE: AGE-RELATED DIFFERENCES IN MICE.

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Aims: Given evidence for age-related differences in effects of drugs of abuse, surprisingly few studies have explored effects of opioids in adolescents (versus adults). This study compared locomotor sensitization in adolescent and adult mice after a single exposure to morphine.
Methods: Adolescent (postnatal day 29) and adult male C57BL/6J mice were treated with saline or morphine (1-100 mg/kg) (session 1), and morphine (10 mg/kg)-induced locomotion was assessed 3-36 days later (session 2). Injections were given i.p. (n=8-10/dose) immediately before each 60 min session.
Results: Morphine during session 1 dose-dependently enhanced the locomotor-stimulating effects of 10 mg/kg morphine during session 2. The minimum significant dose was 3.2 mg/kg in adults and 32 mg/kg in adolescents, and the maximal enhancement was 200% in adults and 150% in adolescents. Irrespective of age, the magnitude of the enhancement increased with the length of the interval between the sessions, attained a maximum at one week, and remained unchanged at two and five weeks. In adults, but not in adolescents, the enhancement was largest when both sessions were conducted in the same environment.
Conclusions: Together, these results show that a single exposure to morphine induced dose-, delay-, and context-dependent sensitization in adult mice. In adolescent mice, morphine induced sensitization less potently, less efficaciously, and less dependent on the context than in adults, but its sensitizing effects were as long-lasting as in adults, and lasted into adulthood.
Financial Support: Supported by DA23261

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DELAY DISCOUNTING RATES FOR ILLICIT, BUT NOT LICIT, DRUGS DEPEND ON DEPENDENCY STATUS AMONG POLY-DRUG RECREATIONAL DRUG USERS.

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Aims: Drug users are known to discount the value of delayed money and drugs of abuse at high rates, resulting in a decision-making pattern biased toward immediate rewards. However, little is known about these drug-specific discount rates for delayed drug rewards in recreational drug users compared to dependent drug users.
Methods: Drug-specific discount rates were collected in a sample of individuals (n=61) who had recreationally used drugs from at least three of the following categories in their lifetime: alcohol, tobacco, heroin, other opioids, barbiturates, sedatives/hypnotics, cocaine, other stimulants, cannabis, and hallucinogens. Discount rates for each drug were compared between participants who met DSM-IV dependence criteria for that drug and those who had tried the drug but did not meet dependence criteria.
Results: As a function of dependency status, discount rates were higher for heroin, other opioids, sedative/hypnotics, cocaine, other stimulants, and cannabis, but were not significantly different for alcohol or tobacco. Insufficient barbiturate- and hallucinogen-dependent participants prevented comparisons with those drugs.
Conclusions: These results demonstrate that the high rates of delay discounting seen with drugs of abuse in drug users are significantly higher in dependent users than in recreational users, but only for the illicit drugs tested. Alcohol- and tobacco-dependent participants did not discount alcohol or tobacco more rapidly than recreational users of these drugs, suggesting that factors beyond dependency status or degree of use may affect drug-specific discount rates.
Financial Support: Institutional start-up funds to WKB.

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CHRONIC METHYLPHENIDATE AND LONG-TERM EFFECTS ON ADULT FEMALE WKY RATS.

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Aims: Animal behaviors are controlled by circadian genes. Drug elicits change in circadian activity pattern indicate that the drug elicits long-term effects. Methylphenidate (MPD) usage is increasing in adult. The study aims to investigate the dose-response characteristics effects of MPD on locomotor circadian activity rhythm pattern of female WKY rats.
Methods: Four groups of female adult WKY rats were used. On experimental day 1 (ED1), all 4 groups received saline injection. On ED2 to 7, each of the 4 groups received either saline, 0.6mg/kg, 2.5mg/kg, or 10.0mg/kg of MPD. ED8 to 10 were washout days. On ED11 the 4 groups were given the same treatment as during ED 2 to 7. Locomotor activity was recorded immediately post injection nonstop for 11 days using 16 open-field assay.
Results: Hourly histograms and statistical cosine analyses calculating the acrophase (Φ), amplitude (A), and mesor (M) were used to assess the 24-hour circadian rhythm activity pattern. During the acute phase (comparing data from ED 2 to ED 1), only the 10mg/kg group showed a significant decrease in the acrophase ($p=0.013$). During the induction phase (ED 7 vs. ED 2), only the 0.6mg/kg group showed a significant increase in activity ($p<0.05$) and activity pattern. In the washout phase (ED 8 vs. ED 1), the 2.5 and 10mg/kg groups showed an increase in activity and statistically significant activity at the same time they had received the MPD injections in the previous 6 days. In the expression phase (ED 11 vs. ED 2), all MPD dose groups alter significantly the locomotor activity pattern.
Conclusions: MPD is currently one of the most prescribed treatments for ADHD and as cognitive enhancement as well for recreation. This study focuses the effects of MPD on adult female WKY rats. Chronic MPD administration alters circadian locomotor activity of adult female WKY rats that is different from adolescent female rats. It also affects the neural circuitry controlling the circadian gene clock. This change in diurnal rhythm pattern activity as a result from chronic psychostimulant exposure is an indication of a long-term effect of these drugs.
Financial Support: NIH RO1 DA027222.

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CHRONIC TREATMENT WITH VARENICLINE DECREASES CONCURRENT COCAINE + NICOTINE SELF-ADMINISTRATION.

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Aims: Clinical reports suggest that cocaine and nicotine are often used concurrently; however, effective medications to treat this form of polydrug addiction are lacking. Varenicline, an $\alpha4\beta2$ nicotinic acetylcholine receptor partial agonist, is FDA approved for smoking cessation. Preclinical studies suggest that varenicline treatment decreases nicotine self-administration, but may increase cocaine self-administration. The goal of the present study was to examine the effects of chronic treatment with varenicline in a nonhuman primate model of simultaneous nicotine + cocaine self-administration.
Methods: Rhesus monkeys (N=3) responded for banana-flavored food pellets (1g) and a cocaine (0.0032 mg/kg/inj) + nicotine (0.0032 mg/kg/inj) combination under a second order (FR2[VR16:S]) schedule of reinforcement during four daily 1-hr sessions. Varenicline (0.004-0.04 mg/kg/hr) was administered intravenously through one lumen of a double-lumen catheter every 20-min for 23-hr each day for 7-10 consecutive days. Varenicline treatment was followed by saline treatment for at least 3 days until food- and drug-maintained responding were at baseline levels.
Results: When cocaine + nicotine was available for self-administration, monkeys earned 97% of the maximum drug reinforcers available compared to 40 and 60% when cocaine and nicotine, respectively, were available alone. Chronic treatment with varenicline dose-dependently decreased cocaine + nicotine self-administration by >50%. Food-maintained responding was not effected and systematic behavioral assessments revealed no evidence of sedation or agitation that would disrupt operant responding. Monkeys returned to baseline levels within a few days after cessation of varenicline treatment.
Conclusions: These preliminary data suggest that varenicline may be an effective medication for concurrent cocaine + nicotine addiction. These studies are still ongoing.
Financial Support: Supported by DA 026892 (NKM) and DA 12001 (FIC) from NIDA, NIH.

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MENTHOL CIGARETTE AND MARIJUANA USE AMONG ADOLESCENTS.

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Aims: Menthol cigarette and marijuana use among adolescents is high; however, little is known about dual use in this age group. Thus, we examined the relationship between cigarette and marijuana use among high-school students and then examined among cigarette smokers the relationship between menthol cigarette and marijuana use.
Methods: We analyzed data obtained from a high school survey (749 non-smokers, 57 sporadic smokers [defined as smoking at least 1 cigarette per day but not daily in the past month], 40 daily smokers) and from a high school-based intervention trial (132 daily smokers) conducted in Connecticut. Chi-square tests were used to assess the differences between smoking statuses (non-smoking vs. sporadic vs. daily smoking) and menthol cigarette vs. non-menthol cigarette use on study variables (demographics, cigarette and marijuana use). Multivariate-adjusted logistic regression assessed the relationship between smoking status and marijuana use in all adolescents and then between menthol cigarette smoking and marijuana use in smokers only.
Results: Compared to non-smokers, smokers (sporadic, daily) were more likely to be male (p=.03) and older (p<.01). Sporadic (OR=9.23; 95% CI: 5.18-16.44) and daily smokers (OR=12.74; 95% CI: 6.15-26.38) were more likely than non-smokers to use marijuana. Of the 229 smokers, 82% of the daily smokers and 18% of the sporadic smokers reported smoking menthol cigarettes (p<.01). Among smokers, sporadic and daily smoking was not associated with marijuana use; however, menthol cigarette smoking, when compared with non-menthol cigarette smoking was associated with marijuana use (OR=1.87; 95% CI: 1.04-3.34).
Conclusions: Smoking cigarettes is associated with marijuana use, and menthol cigarette smoking further increased the odds of marijuana use. Future research is needed to understand neuropharmacology and social norms surrounding the promotion of dual use to inform prevention and treatment of substance use, as well as public health policy surrounding menthol cigarettes and marijuana.
Financial Support: P50DA09421and R01DA026450

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METHYLPHENIDATE FOR ADHD IN ADULTS WITH SUBSTANCE DEPENDENCE: A 24-WEEK RANDOMIZED PLACEBO-CONTROLLED TRIAL.

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Aims: The aim of this trial was to test the efficacy and safety of 180 mg OROS methylphenidate for treating ADHD in patients with amphetamine dependence. The primary end point was relapse to any illicit drugs measured by urine toxicology. Secondary endpoints included relapse to amphetamine use, change in self-rated ADHD symptoms and retention to treatment.
Methods: This was a double-blind trandomized placebo-controlled trial with parallel groups design. .
Fifty-four incarcerated men, 18-65 years, meeting DSM-IV criteria for amphetamine dependence and ADHD, were randomized to MPH or placebo. The trial duration was 24-weeks. The medication started within two weeks before release from prison and continued in outpatient care with twice weekly visits. All subjects received once weekly cognitive behaviour therapy targeting relapse prevention.
Results: The MPH treated group had significantly fewer drug positive urines compared to the placebo group, fewer amphetamine positive urines and better retention to treatment. Compared to the placebo group, the MPH group significantly reduced their self-rated ADHD symptoms during the trial.
Conclusions: This is, to our knowledge, the first randomized clinical trial to demonstrate the efficacy of a stimulant treatment for ADHD in individuals with substance dependence. The results of the study indicated that treatment with MPH led to a reduction in drug use and an improvement of ADHD symptoms in severely dependent individuals.
Financial Support: The trial was supported by the Swedish National Board of Health and Welfare, the Swedish Research Council and Stockholm County Council. Trial registration.

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TAMPER-RESISTANT PROPERTIES OF OXYCODONE DETERX: INTRANASAL ADMINISTRATION AND *IN VITRO* TAMPERING STUDIES.

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Aims: Oxycodone DETERx is a multiparticulate, extended-release (ER), tamper-resistant formulation designed to retain ER properties following common methods of tampering such as crushing, chewing, and preparation for IV injection. The small size of the DETERx beads (median diameter ~300 μm) allows them to be administered by sprinkling or via feeding tube for medical use; this size also makes it feasible to snort for non-medical use. In this study, plasma concentrations achieved in rabbits following intranasal administration of DETERx beads were compared with a non-tamper-resistant reference (original OxyContin OC). In order to assess the effect of tampering on drug release rate, *in vitro* crushing and dissolution studies were also conducted.
Methods: A single-dose pharmacokinetic study was conducted in female New Zealand White rabbits. DETERx beads or crushed reference tablets containing 2 mg oxycodone were introduced intranasally with a puff of air (N=6 per group). Separate *in vitro* studies assessed the effect of 10 household tampering tools (eg., hammer, coffee grinder, mortar and pestle) on drug release.
Results: Intranasal delivery of DETERx beads in rabbits resulted in lower C_{max} and lower early plasma exposure compared to crushed OC tablets; mean C_{max} was 3.5 times lower and mean $AUC_{(0\text{-}2)}$ was 3.4 times lower. DETERx beads also exhibited a longer elimination half-life than crushed OC (mean half-lives of 3.1hr and 0.8hr, respectively). In the *in vitro* studies, dissolution demonstrated that crushed DETERx retained ER properties for all tools tested.
Conclusions: The results of the rabbit study suggest that DETERx retains ER properties when dosed intranasally compared with crushed OC. Together, the studies presented demonstrate robustness of the DETERx formulation ER mechanism in an animal model of snorting and when subjected to tampering by physical manipulations. The Oxycodone DETERx formulation may afford decreased abuse liability through its tamper-resistant properties offering a new approach to mitigation of the recreational drug abuse public health issue.
Financial Support: Collegium Pharmaceutical, Inc.

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INCREASED CONDOM USE WITH PSYCHOLOGICAL ABUSE AMONG DRUG-ABUSING WOMEN IN TEHRAN.

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Aims: Drug abuse, violence victimization, and risky sex are interrelated health problems. We examined abuse and risky sexual behavior in drug-abusing women in Tehran, Iran.
Methods: 120 drug using women were recruited from a rehabilitation center in Tehran in 2009. Women reported sexual behavior for the last 12 months (condom use and multiple partners categorized as <5, 5-10, and >10), and reported abuse using the Revised Conflict Tactics Scale (CTS2). We conducted bivariable and multivariable analyses in SAS.
Results: In unadjusted analyses, psychological abuse was positively associated with condom use (mean abuse score 2.92 vs. 2.17 for any vs. no condom use, p=0.01). In assessing possible confounding, we found higher condom use among younger women (mean age 29.4 vs. 32.7 for users vs. non-users), unmarried women (51.5% vs. 43.0%), women with more sexual partners (37.4%, 66.7%, and 100% for <5, 5-10, and >10 partners), and ecstasy users (38.9% vs. 15.4%). Psychological abuse scores were higher for younger women (r=-0.28, p=0.004), women with more sexual partners (2.46, 2.74, and 2.96 for <5, 5-10, >10 partners) and ecstasy users (2.80 vs. 2.44). In multivariable models, the odds ratio for condom use relative to a one-point increase in psychological abuse was reduced from 1.43 (p=0.01) to 1.32 (p=0.06) when controlling for age, and 1.32 (p=0.10) when controlling for age, marital status, ecstasy use, and multiple partners.
Conclusions: Drug-abusing women who have multiple partners may be more likely to use condoms, and experience psychological abuse. It is possible that residual confounding may partially underlie our adjusted association of 1.32. However, our results point to a set of adverse circumstances and risky behavior in these women, with low control in abusive relationships.
Financial Support: Tehran University of Medical Sciences, School of Public Health, Health Education and Health Promotion Division; and by NIH grant U10DA013727 (PI Brady).

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QUALITY OF HIV CARE AND MORTALITY IN HIV-INFECTED PATIENTS WHO USE DRUGS AND ALCOHOL.

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Aims: To assess whether receipt of HIV care quality indicators (QIs) is associated with mortality in HIV-infected patients who use drugs and alcohol. We hypothesized that higher quality of care (QOC) would be associated with lower mortality in patients with illicit drug and unhealthy alcohol use.
Methods: We surveyed a cohort of HIV-infected veterans enrolled in the Veteran's Aging Cohort Study about substance use and abstracted 9 national HIV quality indicators (QIs) from medical records at baseline. We assessed associations between the percent QIs received and overall, HIV-related, and non-HIV-related mortality using Kaplan Meier survival analysis and Cox proportional hazards models adjusted for age, gender and race/ethnicity, stratified by past year illicit drug and unhealthy alcohol use (AUDIT-C score ≥4).
Results: The majority of the 3,410 patients were male (97%) and african-american (67%) with mean age of 49.1 (SD 8.8) years at baseline. Overall, 22% reported past year illicit drug use and 26% had unhealthy alcohol use. During 15,013 patient-years (PY) of follow-up (mean 4.40, SD 1.45 years), those who received ≥ 80% of QIs at baseline experienced lower overall mortality (4.35 vs. 6.40/100PY; HR=0.58, 95% CI 0.49-0.67), HIV-related mortality (1.91 vs. 3.21/100PY; HR=0.55, 0.44-0.69), and non-HIV-related mortality (2.44 vs. 3.19/100PY; HR=0.60, 0.48-0.74). Overall mortality rates were lower for patients with ≥ 80% of QIs in those with drug (4.94 vs. 6.96/100PY; HR = 0.66, 0.51-0.86) and unhealthy alcohol use (4.27 vs. 6.66/100PY; HR = 0.57, 0.43-0.76), mirroring improvements in non-users. Associations were attenuated after additional adjustment for disease severity.
Conclusions: Higher HIV QOC is associated with improved survival in HIV-infected patients with drug and unhealthy alcohol use. Interventions to improve QOC may improve survival, and help close gaps in QOC for those with substance use.
Financial Support: NIAAA U10AA013566, NIDA K23DA019809

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ANTI-METHAMPHETAMINE VACCINE ATTENUATES REINSTATEMENT OF CONDITIONED PLACE PREFERENCE IN MICE.

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Aims: Previously, we showed that an anti-methamphetamine (MA) vaccine constructed with a large carrier protein (keyhole limpet hemocyanin) using monophosphoryl lipid A as the adjuvant was capable of reducing some conditioned rewarding effects of MA in mice. Now, we test whether a vaccine made with a smaller carrier protein (tetanus toxoid; TT), and an adjuvant approved for human use (alum) can alter the acquisition or reinstatement of MA conditioned place preference (CPP).
Methods: Succinyl MA was conjugated to TT and administered with alum to one set of BALB/c mice (VAX) with a booster given 2-wk later. Another set of mice received TT injections and served as controls (CTL). At 8-wks, three separate groups of VAX and CTL mice (n=10 ea) were trained in MA place conditioning with 0, 0.5, or 2.0 mg/kg MA using an unbiased procedure. CPP, or time spent in the MA-paired side compared to time in the vehicle-paired side, was assessed after 8 training trials (4 MA; 4 vehicle) in a 30-min test conducted drug-free. Four active extinction sessions followed. After confirming MA CPP was extinguished, a test of MA-induced reinstatement was conducted. In this session, mice were administered the MA training dose prior to the CPP test.
Results: Serum antibody levels reached peak levels by 6-wks and remained at a high level throughout the 5-wks of CPP training and testing. MA supported CPP, $P<0.02$, but this effect did not differ between VAX and CTL groups. Among CTL groups, MA reinstated extinguished CPP in the low dose (0.5 mg/kg), but not in the high dose (2.0 mg/kg) group, $P<0.05$. MA did not reinstate CPP in the VAX mice, $P<0.05$.
Conclusions: This anti-MA vaccine constructed with TT and alum that can be used in humans produced high and sustained levels of antibodies in mice. It also blocked the reinstatement, but not the acquisition, of MA CPP. Studies are underway that will test this vaccine construct in rats using other behavioral procedures.
Financial Support: Alkek Foundation; DP1DA033502

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WHICH COMES FIRST, PRESCRIPTION OPIATE MEDICATIONS OR HEROIN?

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Aims: Background: Increased opiate prescription medication availability has led to concerns that opiate prescription drug misuse will lead to heroin use. Aim: For injection drug users who have used both opiate prescription drugs and heroin, we examined trends in which drug was used first by birth cohort.
Methods: Methods: As part of a mixed method, exploratory study on injection drug initiation, quantitative interviews were conducted with injection drug users recruited in community-settings in Los Angeles and San Francisco (N=549) during 2011-12. Interviews covered demographics, family history, drug use and drug injection initiation among others domains. For this analysis, we restricted the study sample to those who reported ever engaging in heroin use and nonmedical use of prescription opiates (n=347).
Results: Results: The overall sample was 33% White, 32% Black, 25% Latino, 27% female, and 60% homeless. Mean age was 46.9 (IQR 41, 56) and mean years of drug injection were 24.8 (IQR 13, 36). Mean age at first illicit drug use was 13.8 (IQR 12, 15) and mean age at injection initiation was 22.1 (IQR 16, 26). The percent who reported having used prescription opiate medications before having used heroin increased for each decade of birth: 16% pre-1960, 30% in 1960-1969, 37% in 1970-1979, and 68% 1980s or later. In a multivariate nominal regression model, we found that being born in the eighties or later was significantly associated with using prescription opiates prior to heroin ($p<0.001$), while controlling for race.
Conclusions: Conclusion: It is clear that the younger the injection drug user is, the more likely they used prescription opiate medications prior to heroin. This analysis does not confer causality. It also completely misses the picture of all the people who start using opiate prescriptions and do not end up using heroin. However, these data suggest the need for more research on the connection between opiate prescription drug misuse and eventual heroin use and drug injection.
Financial Support: NIDA R01DA027689

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NEURAL CORRELATES OF REWARD AND LOSS PROCESSING IN ADOLESCENT SMOKERS: RELATIONSHIP WITH IMPULSIVITY, RISK-TAKING AND SMOKING CESSATION TREATMENT OUTCOME.

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Aims: Adolescence represents a critical phase in the development of neural circuitry underlying reward and motivation. To date, few neuroimaging studies have examined reward processing during this developmental stage in nicotine-dependent adolescents.
Methods: Twenty-one, 14-18 year old, daily adolescent smokers, who expressed interest in a high-school based smoking cessation study underwent functional magnetic resonance imaging (fMRI) while performing a version of the Monetary Incentive Delay Task (MIDT) that parses prospect, anticipation and outcome phases of reward/loss processing.
Results: Relative to neutral trials, participants demonstrated relatively increased frontostriatal activations during reward/loss prospect and diminished activity in the ventromedial prefrontal cortex (vmPFC) and the left inferior frontal gyrus (IFG) during reward/loss anticipation. During winning outcomes, participants demonstrated increased activity in the anterior cingulate and diminished activity in fronto-polar and left IFG areas. In the losing outcome relative to neutral phases, participants showed increased anterior cingulate activity and also bilateral IFG activation extending to the insula. Ventral striatal activity during anticipatory phases of the MIDT correlated with out-of-scanner measures of impulsivity and risk-taking. In a subgroup of adolescents (n=11) who participated in the smoking cessation program, percent decrease in cotinine levels was positively correlated with posterior cingulate activity during reward anticipation and increased bilateral ventral striatal activity during losing outcomes. All findings were significant at $p<0.05$, family-wise error corrected.
Conclusions: The findings suggest that in adolescent smokers specific regional brain activations underlie different aspects of reward and loss processing, and that individual variations in the neural correlates of reward/loss processing relate importantly to impulsivity, risk-taking and treatment outcome
Financial Support: Supported by P50DA009241

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THE ROLE OF GENDER IN THE ASSOCIATION BETWEEN CHILD MALTREATMENT AND SUBSTANCE USE BEHAVIOR: A SYSTEMATIC REVIEW OF LONGITUDINAL RESEARCH FROM 1995 TO 2011.

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Aims: Gender differences in substance use (SU) behavior across the life span have been noted (Nolen-Hoeksema, 2004; Wells, 2009). These recognized differences in the consequences and etiology of men's and women's SU have led to creation of gender-specific services in an attempt to tailor practices for maximum effectiveness. The experience of trauma, such as child maltreatment (CM), has been proposed as one reason for gender differences in SU behavior (Widom, Ireland, & Glynn, 1995). This systematic review analyzes the role of gender in the association between CM and SU outcomes, among longitudinal papers published between 1995 and 2011.
Conclusions: Few dual-gender longitudinal studies have investigated the connection between CM and SU;of these, only ten papers (57%) examined gender as a moderating variable. Results related to gender differences were mixed. When compared, studies that found gender effects were comprised of primarily white samples, measured CM in earlier developmental periods and utilized measures that captured more severe levels and types of SU in later time periods. Comparatively, the studies that did not identify gender effects, had samples that were more ethnically diverse, measured CM as occurring in a broader time period, had SU outcomes that were more restricted in type and severity, and were more focused on outcomes in earlier developmental periods. This review noted several methodological issues in examining gender effects.
Findings indicate that while longitudinal studies continue to strengthen our understanding of the general connection between CM and SU, we remain unclear about the moderating effect of gender across the life course. Results of this review provide implications for potentially sensitive time periods for gender specific services as well as differences in measurement and sample composition that may help elucidate or inhibit our ability to detect gender effects in future research.
Financial Support: Supported by: NIMH Grant 2 T32MH20010

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RESTING-STATE ACTIVITY IN THE LEFT EXECUTIVE CONTROL NETWORK IS ASSOCIATED WITH BEHAVIORAL APPROACH AND IS INCREASED IN SUBSTANCE DEPENDENCE.

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Aims: Individuals with drug addictions report increased willingness to approach rewards. Approach behaviors are thought to involve executive control processes and are more strongly represented in the left compared to right prefrontal cortex. A link between approach tendencies and left prefrontal activity, however, has not been shown in the resting brain. We hypothesized that behavioral approach measures would correlate with the left executive control network (ECN) and that left ECN activity would be greater in substance dependent individuals (SDI) than controls.
Methods: Twenty-five SDI and 25 controls completed a Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) questionnaire and underwent a resting-state fMRI scan. Group independent component analysis was performed. Template matching identified the left ECN component which was then compared across group using a 2-sample t-test. Next, BAS scores were regressed with signal fluctuations in the left ECN.Thresholds were set at $p<0.005$, with an extent threshold of 35 voxels corresponding to a whole-brain cluster-corrected level of $p<0.01$.
Results: BAS scores were higher in SDI compared to controls ($p<0.003$), consistent with higher approach tendencies. Compared to controls, SDI showed significantly greater activity in the left prefrontal cortex of the left ECN. Across groups, BAS scores correlated with signal fluctuations in the left prefrontal ECN.
Conclusions: Our results extend previous task-based studies showing that approach tendencies are related to the left prefrontal ECN, even at rest. Higher activity in the left ECN in SDI compared to controls suggests that left ECN may be involved in heightened approach tendencies that could contribute to drug-related behavior.
Financial Support: Funding for this study was provided by NIDA grants R01 DA024104 and DA027748.

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INJECTABLE EXTENDED-RELEASE NALTREXONE (XR-NTX) FOR PREVENTING RELAPSE TO OPIOID DEPENDENCE: FINDINGS FROM DIFFERING CULTURES, POPULATIONS & SETTINGS.

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Aims: Examine XR-NTX data from Russia and the USA, outpatient and residential settings, in varying populations, and in criminal justice environments.
Methods: All 15 known published,in press or presented clinical studies of intramuscular XR-NTX formulations for OPD (aggregate XR-NTX-treated N=1,683) were examined for data on efficacy, effectiveness and health economic outcomes.
Results: Findings include:efficacy for maintaining abstinence, improving retention, decreasing craving and preventing relapse for ≥18 mos, including in HIV+ and HCV+ patients; feasibility in recovering health professionals, commercially insured/employed patients and uninsured/public populations; and promising effectiveness in community outpatient, residential and drug court, jail and parole settings.Results were consistent regardless of manufacturer vs. independent sponsorship.Data indicate good generalizability of findings and the applicability of the agent both in societies that have (USA) and do not have (Russia) opioid substitution. Safety and tolerability have been shown, including in HIV+ patients;without clinically significant hepatic impact (even with HCV+), intractable acute pain, overdose or death rates. Analyses show cost effectiveness vs. oral agents, owing to decreased hospital utilization.
Conclusions: XR-NTX is a biologic approach to OPD treatment that,with psychosocial treatment, has been shown to provide consistent and durable in-treatment effects across differing cultures, treatment systems and financing models. Limitations include the need for more controlled, randomized designs; post-completion outcomes data; studies of detoxification and induction. While more research is needed,a three decades-long goal of an extended antagonist formulation is yielding a promising therapy and policy opportunity.
Financial Support: The project was funded by Alkermes, Inc. The Medisorb® preparation used in XR-NTX was developed with support from NIDA (grant R43DA013531) and NIAAA (grant N43AA001002).

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THE RELATIONSHIP BETWEEN TREATMENT FOR SUBSTANCE USE DISORDERS AND STIGMA.

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Aims: Drug and alcohol use are subject to harsh moral judgments. This stigma affects employment, physical and mental health, and has been shown to be a barrier to seeking treatment. Thus, the need to address stigma in substance use disorders (SUD) treatment has been noted in the clinical literature. Aim 1: Examine whether stigma is related to post-treatment substance use (SU). Aim 2: Examine whether TAU for SUD affects stigma.
Methods: We assessed stigma using the Substance Abuse Stigma Scale and SU at baseline, post treatment and one month follow up (f/u) among individuals attending intensive outpatient treatment for SUD.
Results: Baseline sample consisted of 17 Caucasian, predominantly male (i.e. 65%) participants, 34.06 (SD= 12.28) years old. They consumed an average of 7.85 (SD=5.98) drinks/occasion and reported drinking alcohol 15.82 (SD=12.89) days/month and using drugs 13.62 (SD=11.57) days/month in the month prior to admission. Aim I: Higher stigma at baseline was associated with higher stigma at f/u, $r=.86$, $p=.01$. Higher stigma at post-treatment was significantly related to more days of drug use at f/u, $r=.74$, $p=.03$. Aim II: Due to small sample size (i.e. n=17 at baseline, 12 at post-treatment and 8 at f/u), we were underpowered to perform any parametric tests. However, mean stigma score at baseline, post treatment and f/u respectively was 48.35 (SD=4.54), 48.75 (SD=3.11), 48.00 (SD=3.21). Essentially, there was no change on stigma from pre to post-treatment and f/u.
Conclusions: Our preliminary results suggest that stigma may have a detrimental impact on SU and higher pre-treatment stigma may be related to higher stigma at f/u. These results highlight the need for more work on these relationships due to very preliminary findings. Still, our data suggest that stigma may be related to SU and may need to be targeted specifically in treatment.
Financial Support: Brown University Medical School Predoctoral Seed Money Research Grant (Kulesza); 2T32AA007455-26 (Larimer).

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GENDER DIFFERENCES IN ANXIETY SENSITIVITY AND SENSATION-SEEKING IN RELATION TO RISK-TAKING ON THE BALLOON ANALOGUE RISK TASK (BART).

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Aims: Problematic risk-taking behaviors, including substance use, increase substantially during adolescence. Research indicates real world risk engagement is positively related with sensation seeking and negatively related with anxiety sensitivity. However, the Balloon Analogue Risk Task (BART) which measures risk-taking in a controlled laboratory setting has shown inconsistent results with these variables. A factor that needs examination as a moderator to elucidate these relationships is gender.
Methods: 11-13 year olds (45.5% female; 54.5% Caucasian) taking part in a larger longitudinal research study completed self-report measures and behavioral tasks over three waves of data including the Sensation Seeking Scale (SSS-V; Zuckerman, 1994; $\alpha = .69$, $M = .67$, $SD = .26$), the Child Anxiety Sensitivity Index (Silverman, 1991; $M = 28.72$, $SD = 4.82$), and the BART. BART performance as a function of sensation seeking and of anxiety sensitivity was examined separately for boys and girls.
Results: Regression analysis indicated at ages 12 and 13, there was a positive relationship between sensation seeking and risk-taking in girls ($\beta = .21$, $t(110) = 2.31$, $p = .02$; $\beta = .27$, $t(89) = 2.55$, $p = .01$, respectively). For boys, on the other hand, results showed an inverse relationship between anxiety sensitivity and risk-taking ($\beta = -.19$, $t(105) = -1.97$, $p = .05$).
Conclusions: Although generally it is assumed that high sensation seeking and low anxiety sensitivity are uniformly related to risk-taking, our data indicate that risk-taking as measured by the BART may be particularly relevant for high sensation seeking in girls and low anxiety sensitivity in boys. Future research should focus on why these constructs may contribute deferentially to boys' and girls' risk taking, and the implications this presents in the initiation of substance use in youth.
Financial Support: R01 DA018647-01 A1

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EFFECTS OF EXERCISE ON CRAVING AND SMOKING IN THE HUMAN LABORATORY.

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Aims: Exercise decreases craving and withdrawal, enhances mood, and increases the delay to ad lib smoking relative to non-physical activities. Our aim was to expand previous work to assess the relation between differing components of craving and smoking in the human laboratory.
Methods: Experiment 1: 21 smokers engaged in three sessions: control, low-intensity exercise, and moderate-intensity exercise. For each session, participants smoked half a cigarette followed by a 1-hr no smoking period, and then they completed the Questionnaire of Smoking Urges (QSU)-Brief before and after 20-min of exercise or control activities. The QSU assesses anticipation of the positive consequences of smoking and relief from withdrawal.
Experiment 2: 15 smokers were exposed to an ABAB within-subjects design (A=control, B=moderate-intensity exercise). Sessions began as in Experiment 1, but after the 20-min exercise/control period, participants underwent a 2-hr ad lib smoking period.
Results: Experiment 1: Participants displayed significant decreases in craving based on the positive consequences of smoking and relief from withdrawal immediately after moderate-intensity exercise, $t(20)=3.98$, $p<.01$ and $t(20)=2.19$, $p<.05$, respectively. Control and low-intensity exercise did not affect craving.
Experiment 2: Exercise effects on the positive consequences of smoking were replicated, $t(20)=2.05$, $p=.05$, and participants waited longer to smoke after exercise sessions ($M=24.33$ min, $SD=37.36$) than control sessions ($M=3.93$ min, $SD=9.80$), $F=8.37$, $p<.01$. Delays to ad lib smoking after exercise were significantly correlated with participants' post-exercise craving based on the positive consequences of smoking and relief from withdrawal, $r=-.65$, $p<.001$ and $r=-.46$, $p<.05$, respectively.
Conclusions: Moderate-intensity exercise decreased self-reported craving, and lower levels of post-exercise craving were associated with longer delays to ad lib smoking. This relation was stronger for craving based on the positive consequences of smoking relative to relief from withdrawal, which supports a multidimensional conceptualization of craving as it relates to smoking in the human laboratory.
Financial Support: UF Dept. of Psychology.

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EMERGING SYNTHETIC AND NATURAL PSYCHOACTIVE DRUGS IN SOUTH FLORIDA'S CLUB SCENE: USERS' DEMOGRAPHIC AND HEALTH RISK PROFILES.

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Aims: Ecstasy use has stabilized in the past decade, but other drug classes are increasingly prevalent in recreational drug use settings. These include synthetic stimulants, psychedelics, and cannabinoids, as well as natural psychedelic drugs. There is little information about the demographic and health risk profiles of users of these emerging drugs in the United States.
Methods: Eligible respondents (N=243) ages 18 to 39 reported recent use of club drugs and misuse of prescription opioids and/or sedatives. Interviewers administered standardized health risk assessments. Drugs of interest were categorized for analysis: 1) natural psychedelics (e.g., psilocybin mushrooms, salvia), 2) synthetic cannabinoids; and 3) synthetic psychedelics and stimulants (e.g., 2C-x, mephedrone, BZP). Logistic regression models examined demographic and health risk characteristics of users of each category.
Results: Users of natural psychedelics (N=57) were younger (p=.000), more likely to be Latino (p=.003) and less likely to be Black (p=.010), used marijuana more frequently (p=.003), and reported higher levels of substance dependence (p=.032) and mental distress symptoms (p=.015) than non-users. Synthetic stimulant/psychedelic users (N=34) reported more frequent misuse of prescription opioids (p=.002) and sedatives (p=.004) and use of LSD (p=.012), more mental distress symptoms (p=.021) and drug-related psychological (p=.008) and physical health (p=.003) problems, and were more likely to inject drugs (p=.009) than non-users. Synthetic cannabinoid users (N=33) were younger than other participants (p=.017), but did not report elevated levels of other drug use or drug problems. No gender differences were observed for any emerging drug class.
Conclusions: Recent users of synthetic stimulants and psychedelics appear to be at high risk for extensive other drug use, drug injection, and drug-related health problems. None of these health risks were associated with synthetic cannabinoid use.
Financial Support: This research was supported by NIH Grant DA019048

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HABITUATION OF THE REINFORCING EFFECTIVENESS OF SENSORY STIMULI: EFFECTS OF METHAMPHETAMINE AND NICOTINE.

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Aims: Visual stimuli (VS) determined to have primary reinforcing effects are classified as sensory reinforcers to differentiate them from other more biologically important primary reinforcers (e.g. food and water). VS are weak reinforcers and their reinforcing effects rapidly habituate. The psychomotor stimulants methamphetamine (METH) and nicotine (NIC) increase the reinforcing effectiveness of VS. Here, we examined the effects of METH and NIC on the habituation of the reinforcing effectiveness of VS.
Methods: The effects of SAL (n = 9), NIC (0.40 mg/kg, n = 9) and METH (0.75 mg/kg, n = 8) on habituation of reinforcing effectiveness were compared. Phase 1 (10 sessions) examined operant level of responding, phase 2 (10 sessions) examined the effects of drug on the operant level of responding, and phase 3 (10 sessions) examined the combined effects of drug and a response contingent VS on the rate of responding. In all three phases within-session changes in the reinforcing effectiveness of VS were examined by plotting and analyzing responding in successive 8 min epochs of each 40 minute test session.
Results: Both METH and NIC disrupted habituation of reinforcer effectiveness. METH increased the rate of responding at all points of the habituation curve indicating that it both increased reinforcer value and disrupted habituation. In contrast, NIC increased responding only in the latter portions of the habituation curve suggesting that this drug affected responding primarily by disrupting habituation.
Conclusions: Slowing or disrupting normally occurring habituation of reinforcer effectiveness may be an important process which mediates the effects of stimulant drugs on behavior.
Financial Support: This work was supported by DA10588 and DA026600 awarded to Jerry B. Richards.

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WITHDRAWN

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PATTERNS OF ADOLESCENT CHEWING BETEL NUT AND LATER DRUG USE IN ADULTS.

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Aims: The betel nuts chewing are popular in Asia. But, its gateway effect between betel nuts chewing and illegal drug use had not been examined clearly in previous studies. Our studies tried to address the timeline of gateway effect among betel nuts and illicit drug use.

Methods: Secondary Data analyzed from the 2005 and 2009 National Health Interview Survey in Taiwan. We used the data containing personal socioeconomic status and addictive materials information including history of smoking, drinking, chewing betel nuts and material use behaviors for measuring their substance usage pattern.

Results: This study examined the onset age of betel nuts chewing and considered the possible association between betel nuts using and becoming illicit drug use later in adult. Similar with cigarette and alcohol, the betel nuts using onset in the age 18 among illicit drug users was younger than non-illicit drug users in the age 20 ($p<0.001$). Regression shown the relationship between betel nuts onset age and later drug use in adult, odds ratio were 0.92(0.88-0.96; 95%CI) in 2005 and 0.95(0.92-0.98; 95%CI) in 2009. This means the later people first involve with betel nuts chewing, the smaller risk to them to becoming illicit drug users in their adult. Furthermore, each additional year of betel nuts usage duration, there was 1.11(1.09-1.13; 95%CI) odds becoming illicit drug users later in adult.

Conclusions: Although the demographic structure was different between 2005 and 2009, the betel nuts gateway pattern shown consistently among these two years. For adolescents who become daily betel nuts chewer, quitting before 18 years old or decreasing the chewing duration before early adult should be the aim of betel nuts and other addict substance control and intervention.

Financial Support: A grant from the Taiwan Food and Drug Administration (DOH101-TFDA-N-004).

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FREQUENCY OF ALCOHOL USE AND REPORTED ENGAGEMENT IN RISKY BEHAVIORS.

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Aims: Previous research has revealed that adolescents who engage in alcohol use are more likely to engage in other risky behaviors (Cooper, 2002; Halpern-Felsher, Millstein, & Ellen, 1996). However, questions remain regarding how these variables are related. The current study further defined this relationship by investigating the association between frequency of alcohol use and risky health behaviors in a sample of adolescents and emerging adults.

Methods: Participants were separated into frequent (1+ time/week) and infrequent (1-2 times per month) alcohol users. A MANOVA was used to examine reported risky sexual behavior, BMI, and substance use in relation to level of consumption (N = 87, Frequent = 30, Infrequent = 48).

Results: The MANOVA revealed frequent alcohol users were significantly more sexually risky than infrequent users ($p < 0.05$): earlier onset of kissing ($F(1, 85) = 5.53$), French kissing ($F(1, 85) = 6.77$), breast touching ($F(1, 85) = 5.00$), penis touching ($F(1, 85) = 7.09$), vagina touching ($F(1, 85) = 5.73$), oral sex ($F(1, 85) = 10.23$), vaginal sex ($F(1, 85) = 12.03$), sexual impulsivity ($F(1, 85) = 5.51$), and frequency of condom use during oral sex ($F(1, 85) = 7.77$). Additionally, frequent users were more likely to engage in unprotected oral ($F(1, 85) = 5.28$) and vaginal ($F(1, 85) = 5.61$) sex. Frequency of alcohol ($F(1, 85) = 227.11$), cigarette ($F(1, 85) = 16.71$), and marijuana ($F(1, 85) = 14.38$) use was greater among frequent alcohol consumers. Additionally, age of alcohol use onset was younger among frequent users ($F(1, 82) = 12.15$).

Conclusions: These findings indicate that frequency of alcohol use may aid in understanding the likelihood of engagement in additional risky behaviors, and proposes that frequent alcohol users represent an important target population in the prevention of risky behaviors. Future research should work to further examine levels of alcohol consumption that may better predict risk for additional risky behaviors, and how these variables are related.

Financial Support: The study was financially supported by Dr. Sherecce Fields, faculty start-up funds.

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PATTERNS OF PRESCRIPTION AND ILLICIT DRUG USE AMONG YOUNG ADULTS: THE SIGNIFICANCE OF HOUSING STATUS AND INJECTION DRUG USE.

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Aims: Over the past 25 years, misuse of prescription drugs, such as opioids, tranquilizers, and stimulants, among adolescents and young adults has become a primary public health problem. Few studies have examined the relationship between housing status and injection drug use in samples of young adults who misuse prescription drugs. The study aims are to: describe demographic and behavioral characteristics of three groups of young adults who currently misuse prescription drugs - housed non-IDU, homeless non-IDU, and homeless IDU - and report different patterns of prescription and illicit drug use among these three groups.

Methods: Enrollment criteria were: between 16 and 25 years old; misuse of opioid, tranquilizer, and/or stimulant 3 times in past 90 days; and injection drug use, homeless, or polydrug use in past 90 days. A total of 596 participants (293 New York and 303 Los Angeles) were enrolled between 2009 and 2011. Independent variables included: race; sexual identity; social factors during youth; drug treatment; and infectious diseases history. Dependent variables included 90-day misuse of illicit and prescription drugs. Analysis consisted of multinomial logistic regression models comparing differences between housed non-IDU, homeless non-IDU, and homeless IDU.

Results: Housed non-IDUs compared to homeless non-IDUs were significantly less likely to have recently used heroin or methamphetamine or have a history of drug treatment or an STI but more likely to have recently misused prescription stimulants. Homeless IDUs compared to homeless non-IDUs were significantly more likely to have recently used heroin or methamphetamine and to have a history of drug treatment and a STI.

Conclusions: Homeless IDUs could be characterized as the most at-risk group while also engaging in the patterns of prescription and illicit drug use that are most consistent with dependency and negative health outcomes. Heroin use is clearly an important factor in patterns of prescription drug misuse, such as opioids and tranquilizers, among homeless IDUs.

Financial Support: Research supported by NIDA R01 DA21299.

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SPECIFIC MATERNAL SUBSTANCE USE BEHAVIORS LINKED TO CHILD CO-OCCURRING EXTERNALIZING AND INTERNALIZING SYMPTOMS.

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Aims: Past research indicates maternal substance use is linked to children's poor behavioral and emotional health and that children with co-occurring externalizing and internalizing behaviors are at greater risk for maladaptive developmental outcomes. However, it is unclear what proportion of children of substance-using mothers exhibit co-occurring symptoms and what type of substance use behaviors are related to co-occurrence.
Methods: Data were obtained from a follow-up study of mothers re-interviewed 10 years after admission to drug abuse treatment (2009-2011). The Addiction Severity Index measured maternal substance use behaviors and mothers reported on a target child using the Child Behavior Checklist (N=396; approx. 11 yrs, range 6-17 yrs). Five oppositional defiant (externalizing) symptoms and six depressive (internalizing) symptoms (Achenbach et al., 2001) were used to identify underlying externalizing and internalizing patterns with latent class analysis (LCA). Maternal substance use behaviors were added as covariates to assess associations with classes.
Results: LCA identified the 3-class model as best-fitting, characterized by a no symptoms (45%), externalizing-only (47%), and co-occurring externalizing and internalizing (9%) classes. More years of maternal amphetamine use predicted to the co-occurring (β=.08, p<.05, OR=1.08) and externalizing-only (β=.07, p<.01, OR=1.07) classes vs. no symptoms class. Mothers reporting greater days of marijuana use and drug problems in the last month prior to follow-up interview were more likely to have children in the co-occurring (β=.05, p<.05, OR=1.05; β=.12, p<.01, OR=1.12, respectively) vs. no symptoms class.
Conclusions: LCA revealed a small group of children at high-risk for co-occurring externalizing and internalizing symptoms, which may have significant implications for intervention efforts targeting children of substance-using mothers. Mothers reporting recent marijuana use and drug problems may be particularly vulnerable to having children with co-occurring problems.
Financial Support: Supported by NIDA R01DA021183, P30DA016383, & K05DA017648 (PI: Hser)

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THE INJECTION OF BUPRENORPHINE-NALOXONE FILM AMONG PEOPLE WHO INJECT DRUGS: FINDINGS FROM THE AUSTRALIAN POST-MARKETING SURVEILLANCE STUDIES, 2012.

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Aims: To examine the diversion and injection of buprenorphine-naloxone film among people who inject drugs regularly (PWID) in the first year following its introduction in Australia.
Methods: Cross-sectional surveys of PWID were conducted in Jan-Mar 2012 (N=450), Jun-Jul 2012 (N=900) and Oct-Nov 2012 (N=450). Additional data sources included interviews with 52 key experts, Needle and Syringe Program data, and opioid substitution therapy sales data. Outcome measures included: patterns of injection, motivations, characteristics of the market for diverted medication and drug liking.
Results: Sales buprenorphine-naloxone tablets steadily declined in Australia following the introduction of buprenorphine-naloxone film. Buprenorphine-naloxone film was injected by fewer PWID (4-6%), less frequently, compared to buprenorphine-naloxone tablets, mono-buprenorphine, and methadone. Among those who injected, one third (33%) injected their own medication and 49% reported injecting someone else's medication (predominantly another's unsupervised doses). Sharing of medication among friends and partners was more common than buying/purchasing. The proportions of PWID who reported withdrawal symptoms following injection of buprenorphine-naloxone film (19%) were similar to those for mono-buprenorphine (22%).
Conclusions: Drug formulation may minimise abuse liability by injection, and buprenorphine-naloxone film may have additional benefits where doses are administered under supervision. However, drug formulation alone will not deter all injection or diversion. Other measures to reduce risks remain important, such as careful patient selection for unsupervised dosing.
Financial Support: The post-marketing surveillance studies of buprenorphine-naloxone were funded by Reckitt Benckiser. The National Drug and Alcohol Research Centre at the University of NSW is supported by funding from the Australian Government.

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LIVER-RELATED DEATHS IN OPIOID-DEPENDENT PEOPLE IN NEW SOUTH WALES, AUSTRALIA, 1997-2005: CONTRIBUTIONS OF VIRAL HEPATITIS AND ALCOHOL.

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Aims: To examine temporal trends in liver-related deaths, and the extent to which viral hepatitis and alcohol are implicated in liver-related deaths among an opioid-dependent population.
Methods: Records for all people entering opioid substitution treatment (OST) in New South Wales, Australia, between 1997 and 2005 were linked to the National Death Index. Liver-related deaths were those with an underlying cause of viral hepatitis, liver disease or liver cancer. We calculated crude and standardized mortality rates and ratios across time. Underlying liver deaths were examined for indications of viral hepatitis or alcohol in the underlying or contributing causes.
Results: The cohort included 20,896 people, 287,330 person-years of follow-up and 2,619 deaths. The all-cause crude mortality rate (CMR) was 912 per 100,000 person-years (py; 95% CI 877, 947). The standardized mortality ratio (SMR) was 5.3 (95% CI 5.1, 5.5). There were 208 decedents with a liver-related underlying cause of death. The liver CMR was 72 per 100,000py (95% CI 63, 83) and the liver SMR was 9.8 (95% CI 8.5, 11.2). The age- and sex-standardized mortality rate for underlying liver deaths increased from 64 per 100,000py in 1997-1999 to 78 per 100,000py in 2003-2005. Viral hepatitis was mentioned in three-quarters (n=156/208; 75%), and alcohol in 43% (n=90/208), of liver deaths. One-third of liver deaths mentioned both these risk factors (n=73/208; 35%).
Conclusions: Liver-related deaths are increasing among opioid-dependent people and the majority of deaths involve viral hepatitis infection. Increasing the uptake of treatment for hepatitis C is essential to addressing this burden of disease. Hepatitis B vaccination, and screening and brief interventions for alcohol use disorders in OST settings may also be of benefit.
Financial Support: Australian National Health and Medical Research Council: Project grant 455451, Early Career Fellowship to SL and Senior Research Fellowship to LD.

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APPROACH-BIAS AND IMPULSIVITY AMONG ADOLESCENT SMOKERS AND NON-SMOKERS: A BI-NATIONAL STUDY.

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Aims: We investigated differences in approach-bias between smoking and non-smoking adolescents in the Netherlands and US. We hypothesized that smokers would have a stronger approach-bias than non-smokers in both countries, especially among adolescents with low inhibition skills and high scores on impulsivity-related constructs.
Methods: A total of 116 adolescents between 13-18 years old participated. Seventy Dutch (smokers n=33) and 46 American (smokers n=26) adolescents participated. Participants completed a smoking Approach-Avoidance Task (based on the cannabis and alcohol AATs), the Stroop Colour Naming Task, Delay Discounting Task, Balloon Analogue Risk Taking and questionnaires assessing tobacco dependence, smoking behavior and impulsivity. Carbon monoxide confirmed smoking status.
Results: Repeated-measures ANOVA demonstrated that US adolescents were generally more positive than Dutch adolescents towards smoking and neutral stimuli. Contrary to our expectations, there was no difference in approach-bias towards smoking stimuli between smokers and non-smokers. No gender differences or interactions were found. Generally, the Dutch adolescents were negative towards tobacco stimuli. The US adolescents did not have a bias towards smoking stimuli. Hierarchical linear regressions among smokers only showed no moderating role of impulsivity constructs on the relation between smoking and approach-bias.
Conclusions: Surprisingly, there seem to be a difference in approach-bias between US and Dutch adolescents. Dutch adolescents who smoke appear to have more negative bias towards smoking stimuli, whereas US adolescents are neutral towards smoking stimuli. Follow-up data will be available in January 2013, which will show us whether this holds on a longer term and whether adolescents who wanted to quit smoking have a more negative bias than adolescents who do not plan to quit.
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MISSED OPPORTUNITY FOR ALCOHOL INTERVENTION AMONG ARMY MEMBERS RETURNING FROM DEPLOYMENT.

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Aims: Greater understanding is needed of factors associated with post-deployment (PD) identification of alcohol problems, and PD referrals for further alcohol assessment and care. Aims are to determine: 1) percent with positive screen of PD alcohol problem, 2) concordance of provider alcohol assessment and positive screen, 3) factors associated with provider referral for further assessment or service.
Methods: Observational study of Army active duty and reserve component members (N=460,020) who returned from a deployment in FY2008-2011 and completed a PD health assessment and provider interview within 60 days of return. Positive screen of alcohol problem based on alcohol use disorders identification test (AUDIT-C) scores for women ≥ 3, for men ≥ 4 on 12 point scale. Provider assessment was response of 'yes potential problem'. Provider referral for further assessment or service was: primary care (PC), behavioral health in PC, mental health specialty, and/or substance abuse program. Bivariate analysis and multivariate logistic regression on any referral in sample with alcohol problem.
Results: The percent of Army members who screened positive PD was high (from 24.0% to 28.1% by component) but provider assessment of potential alcohol problem was only 16%. Of those whom providers assessed with a problem, 35.8% to 40.9% were referred. Older age group, being female, being enlisted, and positive screen for another behavioral problem were associated with increased odds of a referral.
Conclusions: To increase PD referrals for further alcohol assessment and care, research on providers' view of AUDIT-C results is warranted. Results suggest missed opportunity for early intervention based on positive alcohol screens, including in the presence of other PD problems.
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ASSOCIATION OF MENTAL DISTRESS AND NON-MEDICAL PRESCRIPTION DRUG USE: GENDER DIFFERENCES IN THE NATIONAL MONITORING OF PRESCRIPTION STIMULANT STUDY (N-MAPSS).

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Aims: Female adolescents are at higher risk for misuse of prescription drugs (Young et al, 2012). Mental distress can be a modifiable risk factor for subsequent initiation into psychotropic drug use (Steffenak et al, 2011). The association between mental distress and non- medical prescription drug use in youth across ten US cities was examined.
Methods: Data come from the National Monitoring of Prescription Stimulants Study (NMAPSS) which surveyed youth (N=11048; 10 to 18 years) via an entertainment venue intercept recruitment method. Nonmedical use (NMU) of prescription drugs (stimulants, anxiolytics and analgesics) was defined as use of prescription drugs other than by mouth, use that belonged to someone else, or use more than prescribed. Self reported mental distress (MD) included feeling sad, loss of interest in the last 12 months and feeling worried or stressed for more than 6 months.
Results: Overall, 6.2% of girls and 6.6 % of boys reported any NMU in past 30 days; mental distress was higher for girls (56% vs 44%). Among girls who reported MD, 60% met criteria for NMU compared to 64 % boys. When adjusted for age, race, living with parents, grades, ADHD, suspension in school and use of illegal drugs, girls with MD were statistically more likely than those without to report NMU (OR for girls 2.103).
Conclusions: Increased risk of NMU of prescription drug use was found in girls 10 to 18 years reporting mental distress when compared with boys. Promotion of mental health for prevention of nonmedical use of prescription drugs is highlighted as a modifiable risk factor particularly in young women.
Financial Support: Fogarty International Centre ICOHRTA Training Program in Behavioral Disorders (Grant No D43-TW05811; Sonam O Lasopa, Fellow; LB Cottler, PI)
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NATIONWIDE SURVEY OF COLLEGIATE RECOVERY PROGRAMS: IS THERE A SINGLE MODEL?

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Aims: Substance use disorders (SUD) start in adolescence, making this period critical to SUD onset and progression. Effective treatments exist for youth but relapse is common. For remitted SUD youth wishing to attend college, the high rates of substance use on campus represent a serious threat to continued sobriety. Collegiate Recovery Programs (CRPs) are a model of campus-based recovery support that is growing exponentially (from 4 in 2003 to 29 in 19 states currently) but remain unexplored. Since CRPs start organically, they may differ on key dimensions that must be identified before the model is evaluated.
Methods: An online survey of CRP directors (Nov-Dec 2012) will identify the breadth of models, structures, philosophies and services, student characteristics and aggregate outcomes; 20 of 29 completed to date.
Results: Most CRPs operate in public (vs. private) institutions, free of charge to students; 65% operate for < 5 years with 2 staff (Mdn). Only half have a formal application process, require a minimum abstinence duration or accept students on medication management. None accept mandated students. Half have participation requirements pertaining to both recovery and academics; 39% require a behavioral contract and most monitor students in terms of recovery and academics; few ever conduct urine analysis. Services offered by >75% of programs include 12-step meetings onsite, relapse prevention and life skills classes, and sober social events; 65% offer academic advising, peer mentoring and group counseling. Only 40% offer sober housing. None limit duration of stay. Most CRPs define relapse as 'any drinking or using'. Historical relapse rates range from 0-25% (Md 4.5%); CRP student retention and graduation rates both surpass that of the local institution by 5% and 21% respectively.
Conclusions: Findings suggest some similarities across CRPs but also significant differences in level of organization and structure, and on the breadth of key services (e.g., housing). Our goal is to identify and evaluate core CRP models.
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EFFECTS OF A MORPHINE-CONJUGATE VACCINE ON HEROIN SELF-ADMINISTRATION IN RATS.

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Aims: Vaccines have shown substantial preclinical and preliminary clinical evidence of efficacy for treatment of nicotine and cocaine addiction. As such, vaccination could add important therapeutic options to existing therapies for opioid abuse. Several heroin vaccines have shown some promise in animal models, but findings are very preliminary with respect to immunogenicity, effects on opioid pharmacokinetics, and attenuation of opioid induced behaviors. The purpose of the present study was to examine whether immunization with a novel morphine-conjugate vaccine could reduce the reinforcing effects of heroin using a heroin self-administration (HSA) model in rats.
Methods: Two groups of rats (N=8 vaccinated, N=6 controls) were injected i.p. with M-KLH (morphine conjugated via a tetraglycine linker at C6 to keyhole-limpet hemocyanin) or KLH alone in Freund's adjuvant every three weeks. One week after the third injection, rats were given access to heroin (0.06 mg/kg/infusion) during daily 2 hr sessions under a fixed-ratio (FR) 1 schedule for 10 sessions, followed by five sessions each at FR 2 and FR 3. Then, the heroin unit dose was decreased every five sessions to 0.03, 0.01, 0.003, and 0 mg/kg/infusion to obtain a heroin dose-response curve.
Results: Vaccinated rats showed significantly higher mean rates of HSA for the training dose at FR 3. During the dose-reduction phase in rats that had acquired HSA (all but one vaccinated rat), extinction occurred in the majority (5 of 7) of vaccinated rats at unit doses below 0.03 mg/kg, while all control rats showed robust self-administration at all doses. Thus, vaccinated rats showed higher median HSA rates at the 0.03 and 0.06 mg/kg unit doses, but lower median rates at the 0.01 and 0.003 mg/kg doses, suggesting a rightward shift in the dose-response curve compared to controls.
Conclusions: Together, these findings show that M-KLH reduced the reinforcing effects of heroin in rats, and that M-KLH has therapeutic potential as an immunotherapy for opiate abuse.
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MONETARY DELAY DISCOUNTING IN A BEHAVIORAL ADDICTION SAMPLE: AN FMRI PILOT STUDY.

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Aims: Pathological gamblers (PG) discount delayed rewards at higher rates than non-problem gamblers implying differential processing of monetary rewards in areas such as the frontal, limbic and ventral striatal brain structures. We present preliminary data from an ongoing functional Magnetic Resonance Imaging (fMRI) study designed to investigate brain responses in PG during monetary reward choice processing.
Methods: fMRI (Siemens Verio 3.0T) was acquired while 6 PGs participated in a delay discounting task.
Results: PGs evidenced significantly greater ($p<.001$, voxel level) amygdala and dorsal prefrontal activity (Amygdala: x=24, y=3, z=-18, t = 7.53, kE=138; dPFC: x=44, y=32, z=40, t = 14.3, kE=650) when they chose delayed reward, but significantly greater striatal (Putamen: x=34, y=4, z=1, t=27.35, kE = 1868, $p < 0.001$; and Insula: x=-38, y=-4, z=4, t=17.96, kE = 1000, $p < 0.001$) activity when they chose immediate reward. Trials were binned into easy and difficult based on proximity to crossover points. Subsequent analyses indicate increased amygdala, dorsal prefrontal, caudate and insula activity was associated with more difficult choice behavior (Amygdala: x=24, y=3, z=-18, t=4.49, kE = 79, $p < 0.009$; dPFC: x=-48, y=47, z=1, t=4.46, kE = 585, $p < 0.009$; Caudate: x=12, y=0, z=18, t=4.70, kE = 806, $p < 0.009$; Insula: x=-36, y=15, z=7, t=6.75, kE = 1298, $p < 0.001$).
Conclusions: The tendency that selecting delayed rewards in PG was associated with more prefrontal activation may reflect a deficit in cognitive perseveration, whereas the tendency to choose immediate rewards may be mediated by increased responses in the striatum. Selection of difficult over easy choices appears to engage both ventral striatal and prefrontal areas. Greater amygdala activation during difficult and delayed reward choices suggests a possible role of emotional responses to monetary rewards among PGs.
Financial Support: Ontario Problem Gambling Research Centre

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ACUTE EFFECT OF ALCOHOL ON INHIBITORY CONTROL AND SUBSEQUENT TOBACCO USE IN YOUNG ADULT OCCASIONAL SMOKERS.

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Aims: Intermittent smokers use tobacco during alcohol consumption, and alcohol use predicts tobacco escalation. Laboratory studies indicate that the magnitude of alcohol-induced impairment of behavioral inhibition predicts alcohol self-administration, suggesting that alcohol's disinhibitory effects impact alcohol consumption. This study will determine if alcohol's impairment of behavioral inhibition mediates the relationship between acute alcohol administration and cigarette self-administration in young adult occasional smokers.
Methods: Nine of 40 subjects in this ongoing study have completed a randomized, placebo-controlled, within-subjects design to determine the effects of 0.0 and 0.65 g/kg alcohol on behavioral inhibition and subsequent ad-libitum cigarette smoking. Performance tasks (i.e. Cued go/no-go and Digit Symbol Substitution tasks) and subjective measures (i.e. Questionnaire of Smoking Urges – Brief, Biphasic Alcohol Effects Scale) are completed before and after alcohol administration, and ad-libitum smoking of preferred-brand cigarettes are measures for 3 hrs post-dose.
Results: Typical alcohol effects have been observed on subjective measures. Cigarette smoking increases after alcohol administration relative to placebo (1.44 + 0.41 vs. 1.11 + 1.31), and the desire/intention to smoke scale of the QSU-B (187.11 + 55.96 vs. 128.67 + 48.95) at 60 minutes post-dose, relative to placebo. Proportion of inhibitory errors on no-go targets following a go cue is higher after alcohol (0.13 + 0.03) compared to placebo (0.11 + 0.03). In addition, modest correlations have emerged between cigarette self-administration and alcohol-induced inhibitory errors on the cued go/no-go task ($r = 0.14$).
Conclusions: These results demonstrate that alcohol decreases inhibitory control and increases cigarette smoking and subjective desire to smoke in young adult occasional smokers. Furthermore, the modest positive correlation between alcohol's effect on inhibitory control and cigarette self-administration suggests that alcohol's effect on inhibitory control may influence cigarette self-administration.
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EXTENDED-RELEASE NALTREXONE OPIOID TREATMENT AT RELEASE FROM JAIL.

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Aims: Heroin and opioid relapse at jail or prison release is typical. Extended-release naltrexone (XR-NTX, Vivitrol; Alkermes Inc.), a long-acting, monthly, injectable mu opioid receptor antagonist, is potentially effective as a re-entry intervention among persons not pursuing opioid agonist treatments. We are investigating the effectiveness of extended-release naltrexone (XR-NTX) vs. Treatment as Usual (TAU) as opioid relapse prevention among persons leaving NYC jails.
Methods: An open-label, randomized control trial of 8 weeks of XR-NTX (Vivitrol, Alkermes Inc.) treatment initiated one week prior to release from jail, vs. TAU, is recruiting N=40 opioid dependent adults incarcerated in NYC jails not seeking methadone or buprenorphine treatment. Community Medical Management follow-up visits occur at 2, 3, 4 (2nd XR-NTX dose), and 8 weeks. The primary outcome is opioid relapse at week 4 (self-report and urine toxicology).
Results: To date, 29 participants have been enrolled and randomized: 15 XR-NTX, 14 TAU. Acceptability of XR-NTX injections is high (14 of 15 participants received a first injection). 4-week follow-up rates are: 60%, XR-NTX; 57%, TAU. 4-week post-release opioid relapse rates are lower among XR-NTX participants: 36% vs. 87% ($p<0.02$). Observed, confirmed opioid abstinence rates are conversely higher: 64% vs. 13%.
Conclusions: XR-NTX treatment to date appears to lower usual rates of opioid relapse and increase confirmed opioid abstinence at release from jail. XR-NTX, with no abuse or diversion potential, may be particularly applicable to correctional and re-entry settings, where evidence-based buprenorphine and methadone treatments are often prohibited or unavailable.
Financial Support: Support: NYU and Michael Saperstein Medical Scholars, Investigator-Initiated Trial Grant Alkermes, Inc (ALKISS-LEE017). Injectable extended-release naltrexone (Vivitrol®) was developed with support from National Institute on Drug Abuse Grant R43DA013531 and National Institute on Alcohol Abuse and Alcoholism Grant N43AA001002.

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PRE-CUSTODY HIV RISKS AS A FACTOR IN THE EFFECTIVENESS OF THE WAY SAFE INTERVENTION.

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Aims: WaySafe is a curriculum-based group workshop for incarcerated offenders in the final phase of substance abuse treatment, designed to increase positive decision-making skills after re-entry for healthy living, including skills for reducing disease risk behaviors. Previous analyses have shown that participants completing Way Safe, compared to those receiving treatment as usual (TAU), improved cognitive skills for avoiding HIV-risky behaviors and planning risk reduction strategies. We next wanted to assess the effectiveness of WaySafe for offenders who differed in terms of gender, pre-custody HIV risk, and mental health.
Methods: The sample included 1055 males and females in 8 prison-based drug treatment programs randomly assigned to participate in WaySafe groups or TAU. Five WaySafe outcome measures (pre and post) included HIV Knowledge Confidence, Avoiding Risky Sex, Avoiding Risky Drug Use, HIV Testing Awareness, and Risk Reduction Skills. Pre-custody HIV risks were measured at intake using the TCU HVHPFORM (injection risk, sex risk, condom attitudes, and HIV/AIDS concerns). Mental health status was assessed with items representing psychological distress (K10; Kessler et al., 2003).
Results: Due to nesting of participants in 8 different programs, multilevel analysis was used to test effectiveness of the WaySafe intervention on the five outcome measures with gender, pre-custody HIV risk and mental health status included as factors. Results indicated that WaySafe was effective for both males and females. The time (pre- and post-test) by group (WaySafe/TAU) interaction effect remained significant for all five WaySafe measures while controlling for gender, mental disorder, and HIV risk.
Conclusions: WaySafe was designed to improve decision making regarding HIV risks and we hypothesized that high risk offenders would especially benefit. However, these results support the generalizability of WaySafe results to a wide range of offenders regardless of gender, previous HIV risk behaviors, and mental health status.
Financial Support: Funding was provided by NIDA/NIH through a grant to TCU R01DA025885.

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MEMORY-ENHANCING FUNCTION OF DRUG REINFORCERS: THE COCAINE PUZZLE.

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Aims: It has been proposed that the reinforcing properties of drugs of abuse are due, in part, to their ability to enhance memory formation. This hypothesis is primarily supported by evidence of enhanced recall in animals and humans treated with d-amphetamine immediately after training on memory tasks. The aim of the current study was to test this hypothesis using cocaine, a drug that clearly reinforces behavior in many species.
Methods: Cocaine (1 - 20 mg/kg, IP) was administered to male Sprague-Dawley rats immediately after training on "win-stay" tasks in an automated eight-arm radial maze. In win-stay, animals are reinforced with sucrose for entering one specific arm that is illuminated by a cue light; entries in non-lit arms are considered mistakes and are not reinforced. Acquisition is analyzed by Analysis of Variance on % correct choices over successive training sessions, and several studies have found that learning of win-stay is enhanced by post-training administration of d-amphetamine.
Results: In Experiment 1 (n = 32), cocaine dose-dependently impaired acquisition. The impairment, however, was attributed to an interference with performance caused by the development of sucrose avoidance. In Experiment 2 (n = 48), rats received a sensitizing regimen of cocaine exposure prior to administration of cocaine during maze learning. Although cocaine sensitization prevented the development of sucrose avoidance, no clear memory enhancing effects were observed. Experiment 3 (n = 48) was performed in sensitized rats using a more difficult version of the win-stay task but, again, cocaine failed to enhance acquisition.
Conclusions: These data lead to three important conclusions. First, cocaine has a profile of action on memory formation that differs from that of d-amphetamine. Second, part of this difference may be due to a wider dose range of cocaine's aversive effects. Third, cocaine sensitization produces significant tolerance to cocaine's aversive side effects. Therefore, from the perspective of effects on memory formation, cocaine displays peculiar reinforcing efficacy.
Financial Support: Natural Sciences and Engineering Research Council of Canada (NSERC)

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PRESCRIPTION OPIOID ABUSE AND RELATED BEHAVIOR AMONG PRISONERS.

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Aims: U.S. prescription drug use is common, second only to marijuana use. Kentucky continues with high rates of non-medical prescription use, particularly prescription opioids in Appalachian Kentucky. Prescription opioid abuse is associated with increasing arrests. However, there is little systematic examination of prescription opioid use in criminal justice settings. The aim of this study is to examine prescription opioid use levels among Kentucky prisoners to understand other drug use and related behavior.
Methods: The ASSIST and TCU Drug Screeners were administered to 337 prisoners. After consent, subjects entered protocols as part of the NIDA CJDATS 2 cooperative agreement. Analysis examined past 3 month drug use and problem behaviors for 3 levels of prescription opioid use: daily (n=86), some (n=91) and none (n=160). ANCOVA and logistic regressions were performed controlling for group differences in age, gender, race, and rural residence.
Results: Daily prescription opioid users were younger (34.2), more female (39.5%), more white (90.7%) and more rural (58.5%). Daily users significantly reported more use of prescription sedatives (71.3% vs. 56% and 15%, p= <.000) than those in the no use or some use categories. There were no differences in other drug use patterns except for those who reported some use of prescription stimulants (p=<.003) and hallucinogens (p=<.035). Daily users were more likely to inject drugs, rate their drug use as more serious, rate themselves as more dependent on drugs, and report that treatment is important. However, there was no difference in previous treatment history.
Conclusions: Findings suggest that daily users of prescription opioids in the criminal justice system are at greater risk for additional substance use and related problems. They are also more likely to report the importance of treatment. Implications for treatment planning, community re-entry and treatment will be discussed.
Financial Support: CJDATS 2 is funded by NIDA in collaboration with SAMSHA and DOJ.

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WILL THE HEALTH CARE HOME HELP TO REDUCE THE HEALTH COST FOR DRUG USERS IN MEDICAID?

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Aims: Drug users in Medicaid often face multiple physical and mental health problems which cost Medicaid millions of dollars annually. We hypothesized that by integrating mental health and primary care services, the Health Care home (HCH) approach might lower the health care cost (cost) among drug users in Medcaid.
Methods: The present study was a secondary data analysis using Missouri's Medicaid data. Eligible subjects incldued CMHC-HCH patients with a serious mental illness; or a mental illness and substance abuse disorder (SUD); or a mental illness and/or SUD, and other chronic physical condition (e.g., diabetes, COPD, and hypertension), in the past 12 months prior to the enrollment in HCH. In the present study, patients who were Medicare and Medicaid dual eligible, continuously Medicaid eligible < 12 months and aged < 18 years were excluded. The final sample consisted of 2640 patients who were diagnosed with SUDs. Due to the non-normality of the data, the differences in the cost before and after enrolling in HCH were examined using the nonparametric Friedman test.
Results: The sample was 59% male and 73% Caucasians, with a mean age of 42 years. 47% of the patients have a primary/ secondary diagnosis of substance dependence. Alcohol has the highest rate of dependence (21%), followed by opioid (7%), and cannabis (6.5%). The sample was 48% schizophrenia and 11% bipolar disorder. Additionally, 47% of patients were diagnosed with hypertension, 39% with COPD, 25% with diabetes, and 11% with cardiac diseases. The median of baseline and 6-month follow-up monthly cost was $2435 and $2282, respective. The cost in the follow-up period was significantly lower than that at baseline (Friedman test = 26.98, p< 0.0001).
Conclusions: The preliminary findings provide important information on the efficiency of the HCH approach. Further analyses will utilize probabilities matching methods to identify a comparison group; the relationship between the cost reduction and quality of care will also be examined.
Financial Support: None

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SEX TRADING, SUBSTANCE ABUSE, AND MENTAL HEALTH PROBLEMS AMONG INDIGENT HIV-POSITIVE WOMEN: IMPLICATIONS FOR HIV TREATMENT, ADHERENCE, AND DIVERSION.

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Aims: Few studies have examined the factors affecting HIV treatment utilization and ARV medication adherence and diversion among indigent, HIV positive substance abusers. This study sought to determine the association of past year sex trading on substance use, mental health, HIV treatment utilization, ARV medication adherence and ARV diversion (the unlawful channeling of regulated pharmaceuticals from legal sources to illicit markets) among a sample of indigent, substance abusing, HIV positive women.
Methods: 204 HIV positive, substance abusing females in urban South Florida completed a comprehensive health and social risk assessment including demographics, substance use and dependence, and mental health status.
Results: Study participants were predominately African American (79.9%), with a median age of 46. Compared to non-traders, past year sex traders were more likely to meet criteria for substance dependence (p=.000) and report homelessness (p=.000). Recent sex trading was also associated with more significant mental health problems including depression (p=.000), anxiety (p=.002), traumatic stress (p=.000), and increased victimization (p=.000). In terms of treatment utilization, sex traders reported less time spent with primary source of HIV care (p=.002) and more difficultly in accessing medical specialists (p=.023). Sex trading was also associated with ARV medication diversion (30.6% vs. 69.4%; p=.007) and lower levels of past month ARV medication adherence (7.1 days missed vs. 12.7 days missed; p=.002).
Conclusions: This is the first study that documents the diversion of ARV medications by HIV positive, substance using women. Our results suggest that sex traders are especially vulnerable to substance dependence and mental health issues, participate in ARV diversion more often, and have less access to HIV treatment and care. Due to the significant health consequences resulting from ARV non-adherence and diversion, these findings have important public health implications.
Financial Support: This research was supported by Grant Number R01DA023157 from the National Institute on Drug Abuse.

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USING PRESCRIPTION DRUG MONITORING DATA TO PREDICT PRESCRIPTION OPIOID MISUSE.

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Aims: To identify possible predictors of elevated risk for "doctor shopping" – the practice of obtaining controlled substances from multiple health care practitioners without the prescribers' knowledge of the other prescriptions - a proxy for opioid analgesic misuse.
Methods: The data used for this analysis is a subset of the New York State Prescription Drug Monitoring Program, and includes opioid prescriptions filled by 881,558 NYC residents in 2010. A case-control study design was utilized to identify those who met the criteria for doctor shopping, defined as visits to three or more practitioners and three or more pharmacies within a 3-month period. We randomly sampled controls who did not meet the criteria for doctor shopping. Controls were matched to cases on age category, gender, and borough in a 1:1 ratio, yielding a final analytic sample of 1,118 patients. A series of binomial logistic regressions were used to predict the odds ratio (OR) of doctor shopping for prescription-related variables, including type of opioid-analgesic, co-prescribing of certain opioid analgesics, and morphine equivalent dose. After exploratory analyses, a series of multivariate logistic models were constructed.
Results: Univariate analyses showed that cases were 2.2 times more likely than controls to have prescriptions for Schedule II drugs (95%CI: 1.54-3.188),and that the greatest association with doctor shopping was receiving prescriptions for both oxycodone and hydrocodone (OR=4.3; 95% CI: 2.83-6.66). Multivariate analyses yielded similar results, indicating that prescriptions for oxycodone and hydrocodone, and prescriptions for Schedule II drugs could be factors that increase the probability of doctor shopping ($p < .0001$).
Conclusions: Using PDMP data, we identified possible predictors for opioid misuse. Patients with prescriptions for oxycodone or hydrocodone, and Patients with prescriptions for schedule II drugs are more likely to be a 'doctor shopper'.
Financial Support: Primm-Singleton Minority Travel Awards Program

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REDUCING SUBJECT BURDEN: IDENTIFYING CRITICAL MEASURES IN HUMAN ABUSE POTENTIAL STUDIES USING FACTOR ANALYSIS.

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Aims: To assess various subjective effects of abused substances, human abuse potential (HAP) studies include multiple measures to assess positive, negative and overall drug effects. Factor analysis is often used to assess the construct validity of a behavioral scale. In this exploratory analysis, we characterized the relationships among subjective measures using factor analysis in order to identify a reduced battery of core measures.
Methods: To determine the overall factor structure of common abuse potential measures, data from 10 scales (eg, 100-pt bipolar Drug Liking, Overall Drug Liking; unipolar High, Good Effects visual analog scale [VAS]) were combined from 19 double-blind, randomized, crossover HAP studies in recreational drug users (N=532). An initial analysis was conducted using Peak Effect of all doses combined ($Emax_d$) for all VAS across treatments; a second analysis was conducted using Emax by dose. An orthogonal rotation (i.e., varimax) was selected to check the possible overlap and uniqueness of the measurements.
Results: Factor analysis for $Emax_d$ identified 3 factors. Factor 1 included the 'global effect' scales such as Drug Liking, Subjective Drug Value, Take Drug Again, and Overall Drug Liking, with the latter 2 scales loading most highly (>0.85). Factor 2 included primarily unipolar scales with the exception of ARCI-LSD, the only variable to load on Factor 3 (0.96). Good Effects and High VAS cross-loaded on to both Factor 1 and Factor 2 (>0.45 for both factors). Similar findings were observed when variables included Emax for all doses, with the exception that ARCI-LSD loaded on to Factor 2 (0.51).
Conclusions: Factor analysis of $Emax_d$ or Emax of subjective drug effect measures showed similar results, with 2 obvious factors emerging. Strong correlations between positive effects measures suggest potential redundancy; therefore, measures selected for use in HAP studies can be reduced. Additional research is required to identify differences between recreational user sub-groups or specific drug class effects (eg, stimulant and sedative users).
Financial Support: Supported by INC Research

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AGMATINE MODIFIES SOME BEHAVIORAL EFFECTS OF METHAMPHETAMINE IN RATS.

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Aims: The polyamine agmatine modulates various abuse-related effects of opioids. In addition, our recent data show that agmatine also attenuates the rewarding effects of the psychostimulant methamphetamine (MA) in rats. However, it is unclear whether agmatine also modulates other behavioral effects of MA.
Methods: MA-induced rectal temperature increase (hyperthermia), food-induced conditioned place preference (CPP), and MA-induced hyperactivity were used to examine the effects of agmatine on these behavioral actions of MA in separate groups of rats.
Results: MA (10 mg/kg, i.p.) elicited a robust hyperthermia in rats and agmatine (10 – 56 mg/kg, i.p.) dose-dependently and almost completely prevented MA-induced hyperthermia. Palatable food induced robust CPP in rats; agmatine (32 mg/kg) at the dose that markedly attenuates MA-induced CPP had no effect on food-induced CPP. Acute MA (0.32 – 3.2 mg/kg) produced a dose-dependent hyperactivity and daily 1 mg/kg MA treatment for 7 days produced robust locomotor sensitization in rats. Agmatine (10 – 100 mg/kg) further increased MA-induced hyperactivity in rats when treated acutely. Daily treatment with agmatine (32 mg/kg) and MA blunted the development of locomotor sensitization.
Conclusions: These results, combined with our previous report that agmatine attenuates MA-induced CPP, suggest that agmatine selectively blocks the abuse-related and toxic effects of MA. Agmatine is widely used as a tonic supplement and its safety is confirmed in clinical settings. These data support the possibility of using agmatine as a pharmacotherapy for MA abuse and neurotoxicity.
Financial Support: This study was supported by a research initiation fund from University at Buffalo.

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CHANGES IN DRUG USE FREQUENCY AS A RECURRENT EVENT PROCESS: ANALYSES ON THE NATURAL HISTORY OF DRUG ABUSE.

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Aims: Individuals with substance use disorders have highly variable patterns of drug use over time, which are thought to differ by drug type. We aim to identify longitudinal determinants of drug use frequency by drug type.
Methods: We used data on the natural history of primary use of heroin, cocaine and methamphetamine(MA) from 5 observational studies. We constructed 4 drug use frequency episode types based on self-reported monthly drug use: abstinence; low use(1-7 days); moderate use(8-23 days) and high use(≥24 days). We fitted multivariate proportional hazards frailty models to determine differences in durations of these episodes, controlling for a range of fixed, incident (occurring within 30 days of episode initiation), cumulative (occurring between drug use initiation and episode initiation) and concurrent (occurring during the drug use episode) covariates.
Results: The study sample included 629 primary users of heroin, 694 cocaine and 474 MA, with a mean 20.9 years follow-up. Heroin users experienced proportionately more high use episodes than primary cocaine and MA users (34.7% vs. 19.8%, 27.1%), however these episodes were shorter than among MA and cocaine users (mean:13.8 vs. 18.1, 18.3 months). Multivariate analysis revealed several key findings: first, abstinence episodes were longest among heroin and MA users, while durations of high use were not significantly different from durations of abstinence among MA users. Second, older age was associated with longer drug use episodes among heroin users (age >45:HR:0.82(0.77-0.89) vs. age≤25); this relationship did not hold for stimulant users. Finally, cumulative past crime was associated with shorter episode durations for each substance.
Conclusions: Heroin users exhibit more stable patterns of use over time than stimulant users, MA users exhibit relatively longer durations of high-frequency use and criminal engagement has a destabilizing effect on the duration of episodes across drug type.
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A MECHANISTIC PK/PD MODEL OF BUPRENORPHINE.

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Aims: Buprenorphine (BUP) is an opioid receptor partial agonist for the treatment of opioid dependence. BUP administration results in pupil contraction and euphoria. This study developed a mechanistic model to describe the relationship between BUP PK and objective and subjective PD responses in man.

Methods: Data was obtained from 12 subjects administered BUP (8 mg) over 24hr. Plasma samples were analyzed for BUP by a validated assay. PD response was assessed through objective (pupilometry) and subjective (VAS for "Drug Liking") measures. PK/PD model development and analysis was conducted in WinNonlin v5.2 using geo-mean PK and PD data. A mechanistic, time-independent, receptor-occupancy mediated PD model was linked to a multi-compartment PK model; linear and nonlinear signal transduction (ST) was evaluated. Assumptions: linear BUP PK; all PD activity due solely to BUP. Model validity was assessed by visual inspection of model pred vs obs pupil diameter following BUP doses of 4, 8, 16, 32 mg obtained from literature.

Results: A two-compartment model best described BUP PK (R^2=0.89), with absorption and elimination rates of 1.11 hr^{-1} and 0.024 hr^{-1}, respectively. A linked PD model incorporating a nonlinear ST (Hill function) and effect site association (k_{on}) and disassociation (k_{off}) rate constants well characterized the BUP-induced time dependent pupil contraction (R^2=0.96) and subject reported VAS scores for "Drug Liking" (R^2=0.92). Effect site k_{on} (ml/ng-hr) and k_{off} (hr^{-1}) were 0.39and 0.68, respectively, for pupil contraction, and 0.65 and 1.46 respectively, for "Drug Liking". The BUP PK/PD model provided a reasonable prediction of the ceiling effect of BUP PD as measured by pupil contraction vs. time compared with literature data (R^2=0.92).

Conclusions: A mechanistic PK/PD model with nonlinear ST was successfully developed to describe BUP opioid receptor partial agonism. Differences in k_{on} and k_{off} rate constants suggest that objective and subjective responses to BUP may occur at different levels of BUP exposure. This model may be useful in describing the pharmacologic activity of BUP across a wide dose and/or exposure range.

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KK-92A, A NOVEL GABA B RECEPTOR POSITIVE MODULATOR, ATTENUATES THE REWARDING EFFECTS OF NICOTINE IN RAT.

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Aims: GABAB receptors (GABABR) play a critical role in GABAergic transmission in the brain, and are thought to be one of the most promising targets for the treatment of drug dependence. GABABR positive allosteric modulators (PAMs) have been shown to exhibit similar effects as agonists in animal models of nicotine dependence with superior side-effect profiles. The present study involved the synthesis of new selective GABABR PAMs, and the assessment of their effects in animal models of nicotine dependence.

Methods: New derivatives of BHF177, a selective and potent GABABR PAM with efficacy in animal models of nicotine dependence, were synthesized. In vitro pharmacology using a CHO-K1 cell line expressing the heterodimeric GABABR comprised of human GABAB(1b) and rat GABAB2 subunits; in vivo drug metabolism and pharmacokinetics (DMPK) of these compounds were characterized to prioritize the candidates. One of the high priority compounds, KK-92A, was assessed in the nicotine self-administration procedure in rats.

Results: Nine active molecules were selected from 240 analogues of BHF-177 based on in vitro microsomal stability and efficacy in multiple cell-based functional assays, including cAMP accumulation, Ca2+ mobilization, ERK activation and a cellular impedance-based (CellKey) assay. Among these compounds, KK-92A showed improved efficacy in the cAMP and Cellkey assays compared to BHF177, and had a similar in vivo DMPK profile. KK-92A (2, 5, 10, 20 mg/kg, intraperitoneal) significantly decreased intravenous nicotine self-administration under fixed- and progressive-ratio schedules of reinforcement in rats, indicating that this compound inhibited both the primary reinforcing and incentive motivational effects of nicotine.

Conclusions: KK-92A, a novel selective GABABR PAM, attenuates the rewarding effects of nicotine in rats. The present results further confirm that GABABR PAMs may be useful antismoking medications.

Financial Support: 2U19DA026838

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INITIATING BUPRENORPHINE MAINTENANCE FOR OPIATE-DEPENDENT HOSPITALIZED PATIENTS: A RANDOMIZED TRIAL.

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Aims: To determine whether offering opiate-dependent persons hospitalized for medical conditions initiation and linkage to opioid agonist treatment (OAT) with buprenorphine/naloxone (Bupe) would increase engagement in Bupe OAT at 6 months.

Methods: Opiate-dependent patients not currently in addiction treatment who were admitted to a general medical hospital were identified by daily chart review of all hospital admissions and clinical interview by addiction specialist nurse or physician. Eligible, consenting patients (not alcohol dependent, no benzodiazepine misuse) were randomized to 5-day Bupe detoxification protocol (DETOX) or Bupe induction, intra-hospital dose stabilization, and post-discharge transition to maintenance Bupe OAT (LINKAGE). Intention to treat outcomes at 6 months included entry into outpatient OAT, days receiving OAT, and OAT retention at 6-months.

Results: Among 119 participants, mean age was 40.1 (±11.8), 85 (71.4%) were male, 50 (42.0%) were non-Hispanic Caucasian, 35 (29.4%) were African-American, and 25 (21.0%) were Latino. LINKAGE and DETOX arms did not differ significantly (all p values > .4) on demographic characteristics.

Compared to those in the DETOX (n=58), participants randomized to LINKAGE (n=61) were significantly ($\chi 2$ = 43.3, p < .001) more likely to enter Bupe (73.8% vs 13.8%) by 6-months. Among persons who entered outpatient OAT, mean buprenorphine treatment days were 93.2 (± 57.0) and 57.0 (± 56.7) in the LINKAGE (n=45) and DETOX (n=8) arms, respectively. 14 (31.1%) of the persons in LINKAGE who initiated suboxone treatment were still engaged in treatment at the end of 6-months.

Conclusions: LINKAGE was able to enroll 75% of these out-of-treatment opiate dependent persons in OAT. Compared to standard inpatient detox, initiation of and linkage to Bupe treatment is an effective means for engaging medically hospitalized patients who are not specifically seeking care for their addictions in long-term opiate Bupe treatment.

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SEPARATE AND COMBINED EFFECTS OF GABAPENTIN AND Δ9-THC DOSES IN CANNABIS USERS DISCRIMINATING Δ9-THC.

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Aims: The aim of the present study is to determine the influence of gabapentin on the interoceptive effects of Δ9-THC in cannabis users. Gabapentin is being tested because recent clinical trial data indicate that it is effective at reducing cannabis use in dependent individuals seeking treatment.

Methods: The interoceptive effects of Δ9-THC are measured using a pharmacologically specific and sensitive drug-discrimination procedure. During a sampling phase, subjects receive 30 mg Δ9-THC, which is identified by a unique letter code (e.g., Drug X). During a control phase, subjects are required to correctly identify when they received Drug X or Not Drug X (i.e., placebo). Finally, a test phase is conducted in which Δ9-THC (0, 5, 15 and 30 mg) is administered alone and in combination with gabapentin (0, 600 and 1200 mg). We hypothesize that gabapentin will substitute for the Δ9-THC discriminative stimulus, and shift the discriminative-stimulus effects of Δ9-THC leftward/upward. Data are analyzed using ANOVA. In addition to the drug-discrimination task, several other measures are collected to determine a profile of Δ9-THC and gabapentin effects, including heart rate, blood pressure, temperature, self-report questionnaires, time estimation, and performance on psychomotor tasks. Five subjects who reported regular cannabis use have completed the protocol; three are enrolled. Recruitment will continue until the target number of subjects have completed.

Results: Drug doses and combinations have been well tolerated in all subjects. To date, Δ9-THC is functioning as a discriminative stimulus and producing effects typical of cannabinoids in humans. Initial results are also consistent with the hypothesis that the effects of gabapentin overlap with Δ9-THC, and that Δ9-THC effects are enhanced when given in combination with gabapentin.

Conclusions: These results suggest that one mechanism by which gabapentin might facilitate cannabis abstinence is producing effects that overlap with cannabinoids, thereby addressing some of the signs and symptoms that reportedly make abstinence difficult.

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DIFFUSION TENSOR IMAGING OF MAJOR WHITE MATTER TRACTS IN ACTIVE AND RECENTLY ABSTINENT METHAMPHETAMINE USERS.

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Aims: Methamphetamine has been a popular recreational drug for decades. Diffusion tensor imaging studies in abstinent methamphetamine users have found reductions in fractional anisotropy in frontal white matter, suggesting axonal injury and inflammation. To date, no tractography studies have been carried out in participants with methamphetamine addiction; therefore, this study aimed to investigate microstructural changes within 18 major white matter tracts of active and recently abstinent methamphetamine users.
Methods: Imaging was undertaken using a 3.0 T Siemens Magnetom Skyra system and a diffusion-weighted echo-planar imaging sequence with b=1500 s/mm2 and 64 directions. Data were acquired from 11 active methamphetamine users, 6 recently abstinent users aged 22-45, and compared with 9 healthy controls using the FDT toolbox within FSL 5.0, and TRACULA within FreeSurfer. One-way analysis of variance was carried out to determine differences between groups ($p<0.05$).
Results: Statistical analysis revealed diffusion indices differed significantly in some white matter tracts across the three groups – fractional anisotropy in the right anterior thalamic radiation, axial diffusivity in the left uncinate fasciculus, angular bundle and temporal section of the right superior longitudinal fasciculus, and radial diffusivity in the left corticospinal tract and right anterior thalamic radiation. Post-hoc comparison using Gabriel's procedure indicated that recently abstinent methamphetamine users displayed significantly lower fractional anisotropy and higher diffusivity than current methamphetamine users.
Conclusions: Altered diffusion indices were observed in some white matter tracts of abstinent methamphetamine users, compared to current users, suggesting that microstructural damage may follow drug cessation and abstinence.
Financial Support: Oakley Mental Health Research Foundation

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INDUCTION ONTO EXTENDED-RELEASE NALTREXONE IN 302 COCAINE-DEPENDENT OPIOID USERS.

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Aims: The National Institute on Drug Abuse Clinical Trials Network launched the Cocaine Use Reduction with Buprenorphine study in cocaine-dependent opioid users. Subjects were inducted onto 380 mg extended-release injectable naltrexone (XR-NTX) and randomly assigned to buprenorphine/naloxone (BUP) or placebo to assess the effect of BUP on cocaine use. Our aim is to describe the XR-NTX induction process and associated complications.
Methods: Eligibility criteria include being cocaine dependent (DSM-IV), having DSM-IV past-year opioid dependence or abuse or past-year use (self report) and a lifetime history of opioid dependence (DSM-IV), being opioid detoxified per study physician's assessment, and having a pre-induction urine drug screen (UDS) negative for opioids. Subjects were given a Naloxone (NAL) challenge of $\geq$ a 0.8mg injection. If no opioid withdrawal symptoms were noted, oral naltrexone (ONX) (total 50mg) was administered. Again, if no signs of withdrawal were seen, XR-NTX was administered to provide one month of opioid blockade.
Results: 712 subjects consented. 78 subjects did not have a valid UDS negative for opioids and were not eligible for NAL. 317 received NAL. 314 received ONX, and one adverse event of withdrawal symptoms was reported after ONX. 302/317 received XR-NTX, for a 95% completion rate. The median time from NAL to XR-NTX was 2 hrs, with 75% receiving it within 24 hrs.
Conclusions: Relying on both objective (UDS) and subjective (self report) measures was adequate to identify cases able to receive NAL. Utilizing the NAL challenge allowed testing the no-use self report with the objective UDS in a clinical setting where precipitated withdrawal would be short lasting and medically manageable on an outpatient basis. Induction time variation reflected differences in site procedures. A structured approach in a population of cocaine-dependent opioid users proved to be safe and efficient to induct subjects onto XR-NTX.
Financial Support: NIH contracts HHSN271200900034C, HHSN201201000024C

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SCAIFE ADVANCED MEDICAL STUDENT CLERKSHIP IN ALCOHOL AND OTHER DRUG DEPENDENCY: DESCRIPTION AND OUTCOME DATA.

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Aims: The Scaife Clerkship is an intensive three-week summer training experience in the addictions for students between their first and second year of medical school. The Clerkship offers a unique educational and training opportunity in addictions designed to address the gap in medical student education on the science of addiction. Currently, medical students receive little to no training in addictions as part of the regular curriculum, despite the fact that most medical doctors can expect to frequently encounter patients with problematic substance use and/or addictions. The Clerkship curriulum includes lectures, on-site observation, and contact with addiction treatment providers and patients. The program began in 1990 and has expanded and flourished over the years, reaching over 100 students from over 50 different schools across the country.
Methods: Since 2008 we have collected evaluation data on the Scaife Clerkship. Students complete two instruments that measure perceptions and attitudes toward patients with alcohol and other drug problems both before and after the three-week clerkship experience.
Results: Data from both before and after the clerkship experience were available for 56 students. All the subscales of the perception and attitudes instruments were significantly higher after the clerkship compared with before the experience.
Conclusions: Scaife Advanced Medical Student Clerkship in Alcohol and Other Drug Dependency addresses an important gap in medical student education, and provides an intensive educational experience to early medical students in addictions. Evaluation data indicates that students' perceptions and attitudes toward patients with drug and alcohol problems improves significantly as a result of the program. The Scaife Clerkship is a unique and enriching opportunity for medical students from across the country to gain knowledge and experience in addictions, and to apply these new insights in their work as physicians.
Financial Support: This program is funded by the Scaife Family Foundation.

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COCAINE USE REDUCTION WITH BUPRENORPHINE (CURB): STUDY METHODS AND PARTICIPANT CHARACTERISTICS.

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Aims: Recent trials suggest the potential efficacy of buprenorphine/naloxone (BUP) for reducing cocaine use in opioid dependent adults. CURB, a NIDA Clinical Trials Network investigation, is examining the safety and efficacy of BUP given with extended-release injectable naltrexone (XR-NTX) for cocaine dependence in an 11-site, double-blind, placebo-controlled study. This presentation describes participants and study procedures.
Methods: Participants who met eligibility criteria, including a DSM-IV-TR diagnosis of cocaine dependence, and current/past opioid dependence/abuse or past year use and dependence history, received XR-NTX and were randomized to 1 of 3 conditions (sublingual BUP 4mg/16mg per day, or placebo) provided for 8 weeks with weekly CBT. Thrice weekly clinic visits included medication administration and collection of data and urine samples, with follow-up assessments at 1- and 3-months post-treatment.
Results: 712 individuals were consented. Of 302 randomized participants, 78% were male, 63% African American, 26% White, and 10% Hispanic. Mean age was 46.3 years. Participants reported 18.2 mean years of cocaine use, 9.7 mean days of cocaine use in the prior 30 days, 24% met opioid abuse, and 69% met opioid dependence criteria.
Conclusions: Recruitment was completed early, suggesting high interest and acceptance of this treatment approach. Analyses of baseline data documents wide variation in participant characteristics and an appropriately diverse sample from which to generalize to the larger cocaine-dependent population.
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INSIGHT AND MOTIVATION IN DRUG TREATMENT FOR OFFENDERS: A CONTENT ANALYSIS.

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Aims: Insight and motivation have been found to be key factors in successful treatment outcomes in drug treatment for offenders (Garner, et al., 2006). This study sought to examine empirical literature from peer-reviewed journals examining insight and motivation for participants in drug treatment programs with criminal histories. Previous research has often been vague regarding definitions of insight and motivation, and the role these factors play in drug treatment for offenders.
Methods: Articles published in the 21st Century were identified through searches of EBSCOhost databases SocioIndex, and PsychARTICLES. The key concepts entered were: 'motivation;' 'insight;' and 'drug treatment' were paired with the term 'offenders' in varying combinations to identify the ten articles that met the study criteria. Content Analysis methods described by Berg (2001) and Braun and Clarke (2006) were used to analyze the data.
Results: The key concepts of insight and motivation with offenders in drug treatment were implicitly or explicitly defined and examined in the sample. Results of an inductive analysis of the studies major findings revealed these concepts to be significant factors in treatment and treatment outcomes offenders in drug programs. Levels of insight and motivation were classified as either personal or as a goal in the treatment pathway.
Conclusions: Researchers are honing definitions and operationalization of insight and motivation in drug treatment for offenders. Certain studies were able to describe how these factors affect treatment and outcome for this population. A more cohesive conceptualization needs to be implemented in treatment to better serve this population. Recommendations for future research in this growing area, as well as practice and policy implications were discussed.
Financial Support: NDRI Predoctoral Fellow in the BST Program

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WITHDRAWN

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PARTICIPATION IN TEAM SPORTS AS RELATED TO ALCOHOL AND MARIJUANA USE GROWTH IN YOUTH.

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Aims: The aims of this manuscript were to investigate putative mechanisms explaining why those who participate in team sports are at greater risk for alcohol use, but less risk for marijuana use.
Methods: A parallel-process latent growth curve model was used to model both alcohol and marijuana use (vs. non-use). Participation in team sports and gender were considered to be time invariant covariates. The sample consisted of 1,344 youth from the National Survey of Parents and Youth. Data were collected over four yearly rounds.
Results: Analysis revealed that being part of a competitive sports team was related to a lower probability of marijuana initiation, but to increased rates of alcohol use over time. Males had significantly higher levels of marijuana initiation and decreases in rates of alcohol use over time; females had significantly greater rate of increase in alcohol use over time.
Conclusions: Analysis suggests that youth involved in sports are less likely to use marijuana over time. This information may help to uncover other predictors of use over time and to inform policy making as well design as effective prevention.
Financial Support: Preparation of this research was supported by a grant from the U.S. National Institute on Drug Abuse (R01 DA030490).
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COCAINE DEPENDENCE MODERATES THE RELATIONSHIP BETWEEN SEROTONIN TRANSPORTER POLYMORPHISMS AND MEASURES OF IMPULSIVITY.

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Aims: A common serotonin transporter promoter variant (5-HTTLPR) affects the function of the protein; genetic studies indicate that possession of alleles associated with low serotonin transporter function predicts impulsive action in healthy control subjects. Given that cocaine-dependent subjects show higher impulsivity than control subjects, we investigated whether the 5-HTTLPR is related to impulsivity in cocaine-dependent subjects and whether the relationship between the 5-HTTLPR and impulsivity is different between control and cocaine-dependent subjects.
Methods: Two hundred and forty two cocaine-dependent subjects and 98 control subjects were recruited. Impulsivity was assessed using Barratt Impulsiveness Scale version 11 (BIS-11). Demographic data were also collected. DNA was genotyped for the triallelic 5-HTTLPR polymorphism. The serotonin transporter low-expressing S and L(G)polymorphisms were designated S', and high-expressing L(A) was designated L'.
Results: General linear model analysis showed that there was a main effect of group (cocaine versus control, $p<0.01$) and a significant group (cocaine versus control) X genotype (L'L' versus L'S' + S'S') ($p=0.03$) interaction for the BIS total score. Subjects carrying one or two S' alleles had significantly lower BIS scores than those with the L'L' genotype for cocaine-dependent subjects ($p<0.05$), but had higher BIS scores for control subjects.
Conclusions: These results suggest that L'L' genotype is associated with higher impulsivity in cocaine-dependent subjects and that the relationship between impulsivity and 5-HTTLPR is different between control and cocaine-dependent subjects.
Financial Support: P20 DA024157 (Cunningham), P50 DA009262 (Moeller), P50 DA018197 (Kosten), and R25 DA026120 (Chang PI, Liu Trainee) and the Toomim Family Fund. This material is the result of work supported with resources and the use of facilities at the Michael E. DeBakey VA Medical Center, Houston, TX.

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THEMES IN BRIEF INTERVENTION SESSIONS WITH SUBSTANCE-USING EMERGENCY DEPARTMENT PATIENTS: INTERVENTIONISTS' PERSPECTIVES.

Christine Lizarraga, Alyssa A Forcehimes, M Bogenschutz; CASAA, UNM, ABQ, NM

Aims: Interventionists (N=30; 11 male, 19 female) involved in the six-site National Drug Abuse Treatment Clinical Trials Network Screening, Motivational Assessment, Referral and Treatment in Emergency Departments (SMART-ED) protocol delivered 30-minute motivational enhancement therapy-based brief interventions (BI) to patients presenting with problematic substance use during an ED visit. Following the treatment phase of this study, we gathered information on themes in session content that interventionists identified as recurrent. Here we present descriptive information regarding BI session content.
Methods: Interventionists completed a survey that included questions on demographics, affiliated ED, and estimates of the number of interventions delivered. Respondents were asked to describe themes that stood out to them during their sessions as well as to list themes they noticed across different domains (e.g., gender differences). A qualitative approach was used to code and analyze responses.
Results: Twenty-one interventionists (70%) completed the survey. Respondents reported completing an average of 16-20 sessions during the trial. Five interventionists responded that patients seemed highly ambivalent about making a change in their substance use. Eight interventionists reported that most patients did not see their ED visit as related to their substance use. Fifteen interventionists found that patients viewed opioid and IV drug use as more severe/in need of change than marijuana users, although severity and consequences scores were roughly equivalent for these drug classes. Four interventionists noted that females tended to be more aware of and affected by consequences related to their substance use, despite having lower rates of consumption. Finally, six interventionists reported that patients who had previous exposure to treatment were more open to discussions about their substance use.
Conclusions: Interventionists identified recurrent themes noticed during the delivery of the brief intervention. Knowledge of these themes may be useful to those providing substance use interventions in an ED setting.
Financial Support: U01DA015833

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BRAIN SURGERY AND AGONIST ORAL COCAINE: TWO THERAPEUTIC MODALITIES ORIGINATING AND APPLIED IN PERU FOR COCAINE ADDICTION.

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Aims: The use of brain surgery in the form of trepanation to relieve headaches, and use of oral cocaine in the form of chewing coca leaves (chacchado) to decrease fatigue are two methods used for the ancient Peruvians in the Andean regions, and that we have been applying with modern variants since the early 1980s in our region.
Methods: Between 1981 and 1983 performed surgery type bilateral anterior cingulotomy in 33 smoked cocaine as coca paste addicted-patients (Andean addictive form originated in Peru). Since 1980s we have used oral cocaine as agonist therapy contained in coca tea or coca flour over 100 patients addicted to coca paste, under blind or open studies.
Results: Reviewing our studies and their long-term (30 years) results with oral cocaine and brain surgery we can conclude that both treatment modalities offer at least 50% of positive results in patients considered refractory to current treatments.
Conclusions: We hypothesize and suggested the concept of regional therapies: psychosurgery by Incas history, and oral cocaine because only in the Andean regions can buy freely and without legal restrictions oral cocaine containing in coca leaves and its modern industrial products as coca tea or coca flour, which are forbidden outside the Andean regions. Positive statistically results warrants further research in regions where its medical uses is approved for other disorders.
Financial Support: Private support

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EFFICACY OF EXTENDED-RELEASE TRAMADOL FOR TREATMENT OF PRESCRIPTION OPIOID WITHDRAWAL.

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Aims: The study aim was to evaluate the efficacy of extended-release (ER) tramadol in treating prescription opioid withdrawal.
Methods: This was an inpatient, double blind, randomized, three-arm, placebo-controlled trial. Key eligibility criteria included: age 18-55 years old, short-acting prescription opioid use > 20 of the last 30 days, and meeting DSM-IV criteria for current opioid dependence with observed withdrawal. The day after admission, subjects were randomly assigned to oral placebo or ER tramadol (200 or 600 mg daily) for 7 days (Phase 1). Four breakthrough withdrawal medications were available for all subjects. Primary outcomes were: 1) number of breakthrough withdrawal medication doses taken, and 2) subject-rated opioid withdrawal. Secondary outcomes included other withdrawal ratings, subjective measures indicative of abuse liability, physiologic and cognitive measures, and serious adverse events.
Results: Results are reported for the completers (n=12/group). Use of breakthrough withdrawal medication differed significantly among groups [F(4.320); p=0.022]; the 200 mg group received the least amount while the 600 mg group received the most. Specifically, the 200 mg group used less acetaminophen than the placebo group (Dunnett p=0.044). No significant differences among the groups were observed for subjective withdrawal ratings. Only tramadol 600 mg produced significant miosis compared to placebo. There were no serious adverse events, and no significant increases compared to placebo on subjective measures of abuse liability.
Conclusions: ER tramadol 200, but not 600 mg, attenuated opioid withdrawal as evidenced by use of less breakthrough withdrawal medication but not by subjective withdrawal ratings. These data support the continued investigation of tramadol as a treatment for opioid dependence.
Financial Support: NIDA R01 DA027068 (MRL), T32 DA007304 and NCRR and NCATS UL1RR033173.

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CALLOUS AND UNEMOTIONAL TRAITS AS EARLY INDICATORS OF POOR TREATMENT PERFORMANCE IN A BEHAVIORAL ACTIVATION TREATMENT FOR SUBSTANCE-USING ADOLESCENTS.

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Aims: The aim of this study was to investigate how callous and unemotional (CU) traits related to several early indicators of treatment performance among adolescents receiving Behavioral Activation (BA) treatment for substance use in a residential treatment setting. Specifically, we examined the relations between CU traits and motivation to change, activity level, and quality of life over the course of treatment.
Methods: Participants were 110 adolescents aged 13-19 (M = 16.6, SD = 1.2) in residential substance use treatment in New Jersey. All participants were receiving BA as part of their treatment in the center. Participants completed measures upon entry into treatment and 30 days into treatment. Assessment measures included measures of callous and unemotional traits, daily activity level, quality of life, and motivation to change in treatment.
Results: At baseline, CU traits were associated with significantly lower levels of both motivation to change ($r = -.234$, $p < .01$) and activity levels ($\beta = -.27$, $p < .01$), controlling for initial symptoms of depression. Longitudinally, CU traits predicted decreases in motivation to change ($\beta = -.15$, $p < .05$) and was associated with lower levels of quality of life ($\beta = -.15$, $p = .08$) 30 days into treatment, controlling for prior levels of motivation, life quality, and depression levels.
Conclusions: These results suggest that CU traits are associated with important indicators of treatment outcomes in behavioral activation treatment for substance use. Future lines of research include determining whether CU traits predicts treatment dropout as well as designing interventions that specifically target the needs of adolescents with high levels of CU traits.
Financial Support: Not applicable

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THE IMPACT OF GENDER AND MOTIVATION ON PERCEPTIONS OF NONMEDICAL USE OF PRESCRIPTION STIMULANTS.

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Aims: To examine the impact of gender and motivations for use on college student's perceptions of nonmedical use of prescription stimulants (NMUPS).
Methods: College students (N = 696; M age = 18.8; 55.7% female; 81.7% Caucasian) were recruited through psychology department research pools at a medium-sized, mid-Atlantic university (54.4%) and a large southeastern university. Participants were randomly assigned by gender (Subject Gender) to read one of six vignettes that were identical aside motive for NMUPS (study, get high, or lose weight) and the target gender of the college student described as using the prescription stimulant. The target individual described in the vignette was rated on a 14-item semantic differential. A manipulation check was administered to ensure participants accurately recognized the Target Gender and Motive; participants who failed to accurately identify both were excluded (N = 110). Participants also rated the realism of the scenario (1 = not at all; 7 = extremely realistic). Data were collected via survey monkey.
Results: 11.2% of participants reported lifetime NMUPS. Because realism ratings, age, location, history of NMUPS, tobacco and marijuana were significantly associated with semantic differential ratings, these variables were included as covariates in the analysis. A significant target gender by vignette ($F(2, 694) = 3.697$, $p = .025$) interaction indicated that participants rated Male Targets who used NMUPS less negatively if the motivation was to study as compared to losing weight or getting high ($F(2, 307) = 5.075$, $p = .007$). A main effect of Motive suggested use as a study aid was viewed less negatively than the other motives ($F(2, 694) = 6.308$, $p = .002$).
Conclusions: Male Targets are viewed more negatively when the motivation for NMUPS is getting high and losing weight than Female Targets. Overall, students viewed using stimulants nonmedically for a study aid as less negative than using to get high or as a weight loss aid.
Financial Support: Study conducted without financial support

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RELATIONSHIPS BETWEEN POSTPARTUM CIGARETTE SMOKING AND BREASTFEEDING DURATION.

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Aims: The relationship between smoking and early weaning has been established, primarily in epidemiological studies. It has recently been examined in clinical trials where reports from smoking cessation and relapse prevention studies have noted increased breastfeeding (BF) duration with increased abstinence. Other potential moderators of this relationship between smoking and BF should be examined. Among spontaneous quitters (women who quit smoking soon after learning of a pregnancy), our group has reported that delay discounting (DD) predicts postpartum smoking relapse, while educational attainment and depressive symptoms predict smoking status at entry into prenatal care. In the present study, we examined the independent contributions of these three predictor variables of interest (DD, years of education, depressive symptoms) in accounting for individual differences in postpartum smoking and BF status.
Methods: Participants were 111 spontaneous quitters enrolled in postpartum relapse prevention trials. Smoking status was biochemically verified at 24-wks postpartum and self-reported BF status was collected at that same assessment. Significant associations were investigated using univariate and multivariate analyses.
Results: In univariate analyses, older maternal age ($p<.001$) predicted 24-wk smoking abstinence,, greater education ($p<.001$), older age ($p=.002$), and less DD ($p=.01$) predicted continuing to BF, and greater education ($p<.001$) and older age ($p<.001$) predicted combined smoking abstinence and continuing to BF. In multivariate analyses, older age and fewer depressive symptoms independently predicted smoking abstinence ($p<.05$), and greater education independently predicted continuing to BF ($p<.001$) as well as combined smoking abstinence and continuing to BF ($p<.001$).
Conclusions: Younger, more depressed women are more likely to resume smoking. While less DD and more education are each univariately associated with BF, educational attainment is the more robust independent predictor of continuing to BF when examined alone or in combination with smoking abstinence.
Financial Support: R01DA14028, T32DA007242

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SMOKING RISK PERCEPTIONS OF U.S. ADOLESCENTS IN FINE-GRAINED RACE-ETHNICITY SUBGROUPS.

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Aims: To produce detailed special populations estimates for smoking risk perception among 12-17 year olds, stratified by fine-grained race-ethnicity (R-E) subgroup and birthplace, given that 80% of adult smokers in the US start smoking before age 18. These estimates should help guide outreach for prevention initiatives directed toward specific subgroups harboring misperceptions about smoking risk.
Methods: Data are from the US R-DAS National Surveys on Drug Use and Health for 2002-2009, designed to yield nationally representative probability samples of 12-17 year olds (n>120,000), with computer-assisted standardized assessment of perceived risk of daily smoking of 1+ packs (DS1P), current smoking (within 30 days), 15 R-E subgroups, and birthplace. Estimation involved weights and Taylor series linearization approaches for variance estimation.
Results: Estimates are presented for the multiple R-E subgroups, using meta-analysis forest plot summaries. With few exceptions, an estimated 25%-35% of youths under study do not think of DS1P as being a 'great' risk, irrespective of R-E subgroup or place of birth ($p>0.05$). An exception is the foreign-born Japanese subgroup, with a corresponding estimate of 44%, noteworthy due to high smoking prevalence among young foreign-born Japanese (Xue, et al. 2013). Foreign-born Puerto Ricans (PR) and US-born Cubans and PR also have high prevalence of current smoking, but are unexceptional in the DS1P 'great risk' rating (29%-34%). US-born Asian Indians were the subgroup most likely to rate DS1P as a 'great risk'.
Conclusions: Targeted outreach and intervention are indicated for special populations in the US, especially among young Japan-born smokers, for whom disregard for health risks of daily smoking may now drive persistence of smoking. With as many as 25%-35% thinking that DS1P is not a great risk, young smokers in all subgroups under study may benefit from initiatives such as the recent cigarette re-labeling initiatives in Australia and planned for the U.S.
Financial Support: MSU (CLQ, DAB); K05DA015799 (JCA).

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A NEW STANDARDISED MEDDRA QUERY TO ADDRESS DRUG ABUSE-RELATED SAFETY SIGNALS.

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Aims: To develop a new standardised MedDRA query (SMQ) with enhanced sensitivity and specificity to appropriately capture all drug abuse-related safety signals needed for regulatory decisions.
MedDRA is an internationally-used, regulatory classification system of adverse event information associated with drugs and other medical products. Standardised MedDRA Queries (SMQs) are groupings of terms related to a defined medical condition or area of interest, and are intended to aid in case, signal, and trend identification. The current 'Drug abuse, dependence and withdrawal' SMQ was released in 2007. Both regulators and industry have expressed concerns about the adequacy of the current SMQ to identify signals of the evolving prescription drug abuse epidemic. The contextual definitions of misuse, abuse, and diversion are also evolving among academicians, clinicians, industry, and regulators. Our initial needs assessment identified the following challenges, including: overlapping or synonymous Preferred Terms (PTs), inclusion of Lower Level Terms (LLTs) not associated with or available for the respective PT, and inclusion of overly-sensitive or non-specific terms. For example, the PTs Drug abuse, Drug abuser, and Drug dependence all code to different higher level terms (HLTs) and system organ classes (SOCs). These examples highlight the need for an improved SMQ to categorize drug-abuse related safety signals.
Conclusions: As the result of our assessment, and with input from recent efforts to better define the abuse potential terminology used, including the definitions for drug abuse and misuse, we propose a new simplified and concise SMQ to capture abuse-related signals that will provide a framework for harmonized communication among regulators and industry. We anticipate that this new SMQ will result in greater consistency and specificity in the identification, reporting, and interpretation of abuse-related data during the development of psychoactive drugs and in the postmarketing period. Incorporation of this information can aid in the mitigation of product risks and enhance safety for such CNS products.
Financial Support: No disclosures

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DIFFERENCES IN METHAMPHETAMINE USE PATTERNS FOR TREATED AND NOT-TREATED USERS.

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Aims: Most data on long-term patterns of methamphetamine (MA) use are from treatment samples, with few studies of community samples. This 8-year followup study examines MA use patterns for a sample of users with no drug treatment history at recruitment. Based on drug use history from MA-initiation to followup interview, use patterns and user characteristics are compared for 2 subgroups: those with no treatment across their entire history vs. those with treatment between recruitment and followup.
Methods: Data are from a sample of MA users recruited using community outreach approaches, with no drug treatment history at recruitment. Natural History Interviews were conducted in 2001-03 (n=299) and 2009-12 (n=202), including background, health, and risk behavior status and detailed drug use and treatment histories from age 14. Analysis included n=202 who had both interviews. Monthly timelines were constructed with number of days/month with MA use for 15-years following MA-initiation. A mixed effects growth model was used to compare the 2 subgroups (never treated vs. later treated) in terms MA use patterns with selected covariates.
Results: The sample was 36% female; 18% Black, 29% Hispanic, 36% non-Hispanic white, 17% other/mixed ethnicity. Average age was 40 at followup. About 1/3 reported treatment between recruitment and followup. Results indicate similarity of subgroups in terms of initiating MA use at an average of about 10 days per month (intercept) with a general decrease (slope) across the 15-year post-initiation period. However, a significant interaction effect showed that the treated group had higher levels of use (and greater increases) until they utilized treatment. Group patterns were not differentiated by gender, age, injection use, or whether ever incarcerated.
Conclusions: A substantial number of MA users decreased their use over a 15-year period without treatment; however, many of this group did maintain some level of use. Those utilizing treatment experienced decreasing use following treatment. Further exploration of "natural" recovery may identify facilitators and barriers of abstinence.
Financial Support: NIDA DA025113, DA015390, P30 DA016383-06

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EVALUATION OF TRENDS IN ABUSE OF STIMULANTS IN HIGH SCHOOL AND COLLEGE-AGE PERSONS USING RADARS® SYSTEM DATA.

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Aims: Stimulant use, beyond prescribed use, is documented in school-aged persons for performance enhancement. The purpose was to examine trends in stimulant use for high school and college age persons, comparing typical summer and in-school months. The hypothesis was stimulant use would be higher during the school year as some students use stimulants as academic performance enhancers.
Methods: Data from the Poison Center program of the Researched Abuse, Diversion and Addiction-Related (RADARS®) System involving Intentional Misuse and Abuse cases from July 2007 to June 2012 were included in the analysis. Methylphenidate and amphetamines were analyzed separately. Models were performed as rates per 100,000 population and per 1,000 Unique Recipient of Dispensed Drug (URDD). Age groups compared were 14-18 years, representing high school students, and 18-25 years, representing college students. Also compared were summer months (June, July) to in-school months, August through May.
Results: For both age groups and stimulant classes, URDD and population rates in school months were significantly higher compared to summer months. URDD rates were 22.8% [$p<0.0001$] higher and population rates were 26.7% [$p<0.0001$] higher. Population and URDD rates for methylphenidate were higher for high school age persons, 31.0% [$p<0.0001$] and 31.2% [$p\leq0.0002$], respectively. Population and URDD rates for amphetamines were higher for college age persons, 35.5% [$p<0.0001$] and 35.6% [$p<0.0001$], respectively.
Conclusions: Results show seasonal trends for stimulant use: for both high school and college age groups, Intentional Misuse and Abuse rates were 25% higher in school months compared to summer months. Also, rates for two classes of stimulants were different; college age showed higher rates of amphetamine use, while high school age showed higher rates of methylphenidate use.
Financial Support: The RADARS® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscriptions from pharmaceutical manufacturers.

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SUBSTANCE USE AMONG MEDICAL CANNABIS USERS: SUBSTITUTING CANNABIS FOR ALCOHOL AND OTHER SUBSTANCES.

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Aims: We examined cannabis use as a substitute for alcohol and other drugs among medical cannabis users. We aimed to examine the stability of the substitution effect with regard to substance use treatment history and medical conditions.
Methods: Participants were 476 self-selected adults who endorsed current medical cannabis use. Participant completed surveys of attitudes and behaviors related to cannabis use as part of the Cannabis Access for Medical Purposes Survey.
Results: History of substance use treatment was reported by 16% (n=74), of whom 65% (n=48) substituted cannabis for alcohol or illegal drugs; 49% (n=36) substituted for alcohol, 53% (n=39) substituted for illegal drugs, and 36% (n=27) substituted cannabis for both. Rates of substitution were similar across treatment histories; 54% (n=215) of individuals with no history of treatment reported substituting cannabis for alcohol and/or illegal drugs. Substitution was generally consistent across primary illness; patients with cancer, HIV/AIDS, gastrointestinal disorders, epilepsy, mental health, arthritis and chronic pain reported equivalent rates of substitution, whereas patients with MS reported less substitution, 30% (n=6).
Conclusions: These cross-sectional findings suggest that cannabis use is perceived to play an important role in reducing use of alcohol and other drugs among medical cannabis patients. These findings have implications for treatment that encourages abstinence from cannabis in the process of reducing the use of other substances. Findings of consistency for cannabis substitution across illnesses and history of substance use treatment suggests that cannabis use may play a role in moderating substance use across a broad range of adults, and highlights the importance of conducting further research on the complex interaction of cannabis use with use of other psychoactive substances.
Financial Support: This research was supported by a grant to Zach Walsh from the UBC Institute for Health Living and Chronic Disease Prevention.

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MARIJUANA NORMALIZES SLEEP EFFICIENCY IN MARIJUANA-DEPENDENT VOLUNTEERS.

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Aims: Sleep disturbance is commonly reported by chronic marijuana (MJ) users particularly during abstinence and often is identified as a contributor to MJ relapse after treatment. In this study we compared sleep patterns of heavy MJ users after both placebo and active MJ administration to those of normal controls.
Methods: MJ users (4M/2F) were a subgroup from an inpatient MJ discrimination study. All met DSM-IV criteria for cannabis dependence, but were otherwise healthy. Age-matched controls (10M/3F) reported no history of illicit drug use or medical illness. No participants reported symptoms consistent with a primary sleep disorder. Polysomnography (PSG) was conducted from 2300-0700 hr and scored using standard criteria. Placebo (0.0% THC) and active (2.7%THC) marijuana cigarettes were administered twice per day (at 0900 and 1300) on separate days, in randomized and counterbalanced order.
Results: Following placebo smoking, MJ users (relative to controls) demonstrated worse sleep efficiency (SE: sleep time ÷ bed time; 81.2 vs 90.3%, $p<.02$), longer sleep onset latency (SOL; 50.4 vs 16.2 min, $p<.04$) more time in Stage 1 and awake (WASO+1) (153.8 vs 66 min, $p<.01$) and lower percent Stages 3/4 (6.0 vs 15.7%, $p<.03$). Following active MJ smoking, MJ users showed improvement (relative to placebo) on SE (81.2 vs 87.5%, $p=.05$), WASO+1 (153.8 vs 91.7 min, $p<.02$) and SOL (50.4 vs 23.3 min, ns), but not other sleep stages. Except for percent Stages 3/4, which remained low (6.9 vs 15.7%, $p<.04$), sleep pattern following active MJ did not differ from controls.
Conclusions: The data show reduced SE and lightened sleep in abstaining heavy MJ users, which was "normalized" following MJ administration. Persistently reduced Stages 3/4 sleep may be important as this parameter predicts relapse among alcoholics.
Financial Support: NIH R01 DA026761 and Joe Young Sr. Funds (State of Michigan) supported this research.

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WITHDRAWN

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THE EFFICACY OF TOPIRAMATE AT REDUCING ETHANOL'S REINFORCING EFFECTS IS CORRELATED WITH ETHANOL-INDUCED EXTRACELLULAR GLUTAMATE CONCENTRATIONS IN THE NUCLEUS ACCUMBENS OF ALCOHOL-PREFERRING RATS.

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Aims: Topiramate, a GABA/glutamate modulator, has been suggested as a potential treatment for alcohol dependence that should theoretically suppress corticomesolimbic dopamine, and thus decrease alcohol's reinforcing effects and levels of consumption. Results demonstrate that topiramate reduces alcohol consumption in both humans and animal models; however, the bio-behavioral mechanisms that underlie its efficacy have not yet been validated.
Methods: Here we examined the effects of acute topiramate administration (0, 10, 20 mg/kg) on ethanol reinforcement in Wistar rats and alcohol preferring (P) rats using a progressive-ratio schedule. We also examined its effects on ethanol-induced changes in the extracellular concentrations of dopamine [DA], glutamate [GLU], and serotonin [5HT] in the nucleus accumbens (NAc) using in vivo microdialysis and HPLC.
Results: Acute topiramate administration at 10, but not 20 mg/kg, robustly decreased the breakpoint of ethanol maintained responding in P rats, but not Wistar rats. Although topiramate administration reduced ethanol-induced extracellular [DA], the effect does not appear to be related to reduced ethanol reinforcement since similar changes were observed for both doses and both strains tested. Topiramate administration did not significantly affect [5HT] at either dose tested in either rat line. Interestingly, ethanol-induced [GLU] were significantly reduced following 10 mg/kg of topiramate in P rats but not Wistar rats, an effect that was positively correlated with reductions in breakpoints for ethanol self-administration following topiramate administration.
Conclusions: These findings support the hypothesis that topiramate's efficacy is related to its ability to reduce ethanol's reinforcing effects; however, the mechanism of action appears to be mediated by glutamatergic, not dopaminergic, signaling in the NAc.
Financial Support: NIAAA grant R01AA016554 (WJL).

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SMOKING-RELATED PSYCHOPATHOLOGY ACROSS CULTURES.

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Aims: The hardening hypothesis posits that due to anti-smoking campaigns most smokers who have the psychological resources to quit have already done so, leaving the remaining smoking population characterized by poor psychological wellbeing and high nicotine dependence. The current study examined this by assessing mood and trait correlates of heavy smoking in a Western country where smoking is stigmatized, Australia, and in China and Japan where smoking is normative.
Methods: The following groups aged 19-31 years were recruited online and through newspaper ads for paid research subjects: current heavy smokers, i.e., those who smoke at least 20 cigarettes per day and have done so for at least one year; never-smokers, defined as those who have never smoked; and ex-smokers, defined as former heavy smokers who have not smoked for at least one year. Measures included the Fagerstrom Test for Nicotine Dependence (FTND), Depression Anxiety Stress Scales (DASS), Negative Mood Regulation (NMR) scale, Alcohol Use Disorders Identification Test (AUDIT), and Frontal Systems Behavior Scale (FrSBe). The total sample size after deletion of cases with missing data, outliers and those who did not meet criteria was 412.
Results: Among current smokers FTND scores were significantly positively correlated with DASS Depression, Anxiety and Stress, FrSBe Apathy, Disinhibition and Executive Dysfunction, and AUDIT, and negatively correlated with NMR. Multivariate analysis controlling for age and gender indicated that across both samples current smokers scored significantly higher than never-smokers and ex-smokers on DASS Depression, Anxiety and Stress, FrSBe Apathy, Disinhibition and Executive Dysfunction, and AUDIT, and significantly lower on NMR. East Asian smokers reported significantly higher nicotine dependence than Australian smokers, and most differences between smokers and non-smokers were greater among East Asians than Australians.
Conclusions: Findings contradict the hardening hypothesis and are instead consistent with either a pre-smoking trait interpretation or consequences of nicotine addiction.
Financial Support: This research was supported by the Bond University School of Humanities and Social Sciences.

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STRIATAL GATING EFFECT AND PREDICTION OF TREATMENT RESPONSE IN COCAINE DEPENDENCE.

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Aims: This pilot study attempts to address 2 questions: 1. What is the causal (directional) effective connectivity between prefrontal cortex and striatum (STR) in cocaine dependent subjects (CDs); 2. Is striatal gating of cortico-cortico effective connectivity related to response to treatment with dopamine (DA) enhancing medications in cocaine dependence.
Methods: Pretreatment fMRI data during a working memory task were acquired from 6 CDs, who subsequently received DA enhancing medications at least 8 weeks, and 6 controls. Stochastic and nonlinear dynamic causal models (DCM) measured the effectively connectivity among 7 regions of interest: left (L) middle frontal gyrus (MFG), L inferior frontal cortex (IFC), L posterior parietal cortex (PPC), right (R) PPC, bilateral (LR) dorsal STR, LR ventral STR, LR thalamus. Two putative DCMs (a DCM in which MFG causally affects STR, and a DCM in which STR causally affects MFG) were tested. The activity in the dorsal STR was hypothesized to gate (positive modulation effect) the connectivity from L IFC to L PPC, based on O'Reilly and Frank's (2006) working memory model.
Results: Results showed that MFG causally affected STR. The strength of the endogenous connectivity from MFG to ventral STR was lower in CDs than controls. Low pretreatment gating by the dorsal STR (posssibly reflecting low pretreatment DA function) was associated with improvement on the Treatment Effectiveness Score after treatment (r=–0.69).
Conclusions: The lower strength of the MFG-ventral STR connectivity in CDs may reflect low DA function related to decreased prefrontal-striatal glutamatergic neurotransmission. The results are consistent with the theory that DA enhancement may be a useful target for pharmacotherapy of cocaine dependence in CDs who have pretreatment hypodopaminergic state.
Financial Support: Peter F. McManus Charitable Trust Grant (FGM & LM), NIDA Grants #P50 DA009262 & K02 DA00403 (FGM).

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PHARMACOKINETICS AND SUBJECTIVE EFFECTS OF INHALED SALVINORIN A, A KAPPA-OPIOID AGONIST HALLUCINOGEN PRESENT IN THE PLANT *SALVIA DIVINORUM.*

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Aims: Salvinorin A is a kappa opioid agonist and the principal psychoactive constituent of *Salvia divinorum*, which has increased in popularity as a recreational drug over the past decade. Pharmacokinetics and subjective effects of inhaled salvinorin A were examined in 6 psychologically and physically healthy hallucinogen-using adults.
Methods: Each participant inhaled a single high dose of vaporized salvinorin A (*n=2*, 18.0 μg/kg; *n*=4, 21.0 μg/kg). Behavioral and subjective effects were assessed every 2 min for 60 min after inhalation. Blood samples were collected at 13 time points from baseline to 90 min post-inhalation and cold centrifuged to obtain plasma. Plasma samples were purified by solid phase extraction and analyzed in triplicate via liquid chromatography-tandem mass spectrometry using a +5 mass analogue of salvinorin A as internal standard.
Results: Plasma levels of salvinorin A (SVA) peaked at 2 min then rapidly and progressively decreased toward pre-inhalation levels. For each participant, SVA levels strongly correlated with participant ratings of drug strength across time (median *r* value = .93, range = .85 to .99). Repeated measures regression showed that SVA levels were significantly ($p < .01$) associated with participant and monitor ratings of drug strength and monitor ratings of unresponsiveness, distance from usual daily reality and psychological distress. End-of-day questionnaires confirmed intense subjective effects as well as moderate ratings of drug liking/good effects, consistent with previous findings.
Conclusions: This is the first study to demonstrate a direct relationship between changes in plasma levels of salvinorin A and behavioral/subjective effects in humans. The results confirm the efficacy of a vaporization/inhalation technique for studying the effects of salvinorin A across multiple doses and across time.
Financial Support: Conduct of the study was supported by National Institute on Drug Abuse (NIDA) grant R01DA003889. Support for Dr. Prisinzano was provided by NIDA grant R01DA018151.

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DOPAMINE SYSTEMS IN ADOLESCENT AND ADULT BRAIN RESPOND DIFFERENTLY TO METHAMPHETAMINE.

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Aims: Adolescent initiation of methamphetamine (METH) is associated with higher prevalence of addiction, neuropsychological deficits and severe mental health outcomes. Adolescent rodents are more sensitive to the conditioned rewarding properties of METH than adults, reinforcing the view of heightened adolescent susceptibility to METH. We previously reported that METH elicits different locomotor stimulant effects and gene expression changes in regions of adolescent and adult mouse brain. METH decreased expression of axonal guidance molecules (EphB1, Netrin, UNC5a) that guide formation of dopamine pathways in adolescent hippocampus, but upregulated these and other genes in adult hippocampus. Other brain regions also displayed age-dependent responses.
Methods: We investigated whether METH altered: mRNA expression of dopamine receptors, vascular endothelial growth factors with RT-PCR, and markers for dopamine neurons (immunohistofluorescence) differently in adolescent and adult mouse brain regions.
Results: METH: (1) increased mRNA expression of D2, D4, D5 dopamine receptors in adult, but not adolescent hippocampus, (2) reduced expression of select vascular endothelial growth factors in both age ranges, (3) increased the ratio of tyrosine hydroxylase (TH) expression, compared with the dopamine transporter (DAT) in substantia nigra and disrupted fiber tracts more in adolescent than in adult mouse hippocampus and striatum.
Conclusions: Down-regulation of Netrin/UNC5a/DCC conceivably portends METH-induced changes in pubertal development of dopamine circuitry, dopamine receptors in brain regions. Blood vessels support neurogenic processes, regulate differentiation and migration and define functional domains. Changes in vascular endothelial growth factor receptors may also contribute to an altered trajectory of neurodevelopment in the adolescent brain. Our findings, that METH altered dopamine synaptic architecture differently and more robustly in the adolescent than the adult brain, may contribute to increased adolescent susceptibility to the adverse effects of METH.
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DELAY DISCOUNTING OF REMIFENTANIL UNDER A DRUG-DRUG CHOICE PROCEDURE.

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Aims: A drug-versus-drug choice procedure was used to examine the impact of reinforcement delay on responding maintained by the mu opioid receptor agonist remifentanil.
Methods: Rhesus monkeys (n=4) lever pressed under a concurrent fixed-ratio 30 schedule. Responses on either lever delivered an i.v. infusion, either remifentanil or saline. After dose-effect curves were determined when remifentanil was available on one lever and saline was available on the other, monkeys chose between two doses of remifentanil, and the delay to delivery of the larger dose was varied systematically across sessions.
Results: Remifentanil (0.01-1.0 μg/kg/infusion) dose dependently increased responding on the drug lever when the alternative was saline. When given a choice between two doses of remifentanil that maintained responding, monkeys chose the larger dose. When given a choice between a smaller dose delivered immediately (0.032-0.01 μg/kg), and a larger dose (0.32-1.0 μg/kg) delivered after a delay (30-240 s), responding for the larger dose decreased, and responding for the smaller dose increased, as a function of delay.
Conclusions: Responding under this choice procedure was sensitive to both reinforcer amount and delay. In some cases, when the larger dose was delayed, monkeys responded for smaller doses of remifentanil that otherwise (i.e., during the single-lever self-administration study) did not maintain levels of responding above that maintained by saline, suggesting that the context in which drug taking occurs (e.g., changes in the availability of other reinforcers) can influence the reinforcing effectiveness of drugs. The imposition of a delay not only reduces the value of the delayed reinforcers but also increases the relative value of other immediately available commodities (e.g., smaller doses of drug). Enhancement of the reinforcing effectiveness of drugs in the context of other delayed reinforcers might contribute to increased vulnerability for drug abuse among individuals that are more sensitive to reinforcer delay.
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STATE VERSUS TRAIT: EVALUATING THE STABILITY OF NEUROCOGNITIVE FUNCTIONING OVER TIME IN COCAINE-DEPENDENT PARTICIPANTS.

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Aims: The goal of this project was to evaluate whether neurocognitive functioning remains stable, improves, or worsens over time in non-treatment seeking cocaine-dependent participants.
Methods: Using a within-subjects study design, participants were administered the following neurocognitive tests at 3 distinct time points (study visits): Continuous Performance Task (CPT; a measure of attention/information processing), N-Back (a measure of working memory), Hopkins Verbal Learning Task – Revised (HVLT-R; a measure of verbal memory), and the Wechsler Adult Intelligence Scale (a measure of IQ). The order of administration was the same and the assessments were identical with the exception of the HVLT where alternate forms were administered.
Results: The sample (N=22) included cocaine-dependent volunteers who were primarily African-American males aged 44.0±1.1 (mean ± SEM) years. Participants reported using 2.2±0.6 grams of cocaine/day, 17.1±1.9 days out of the last 30 days, and an average of 17.7±1.1 years of use. On average, 117.4±15.5 days elapsed between the administration of the first and second neurocognitive batteries, and 135.2±29.4 days elapsed between the second and third neurocognitive batteries. With regard to the HVLTand N-Back assessments, performance did not significantly differ across the 3 assessments. However, performance worsened over time and/or were variable between sessions for a few CPT indices, including number of omissions, variability, hit rate standard error, and hit rate block change.
Conclusions: Performance on measures of neurocognition, particularly episodic and working memory, appear to be consistent over time. These findings reflect, in the absence of any intervention or other acute event, stability of neurocognition in this cohort. Furthermore, with respect to the psychometric properties of the battery, the results show that these assessments are not susceptible to practice effects.
Financial Support: This work was conducted at the MEDVAMC, Houston, TX. Funding from NIH grants: DA023624; DA028387; DA023588.

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POORER PARENTAL MONITORING IS ASSOCIATED WITH COCAINE EXPOSURE IN EARLY ADOLESCENCE IN GIRLS BUT NOT BOYS.

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Aims: To study the degree to which early adolescent cocaine exposure (EACE) is associated with parental monitoring (PM), with attention to male-female differences and holding constant prenatal cocaine exposure (PCE).
Methods: Participants were enrolled at birth in the longitudinal Miami Prenatal Cocaine Study. As part of the 12-year follow-up exam, 204 girls (114 PCE) and 198 boys (95 PCE) were studied. PCE was assessed by maternal self-report and drug assays; EACE solely by drug assays. Log odds of EACE have been regressed on self-report caregiver PM, based on standard multi-item scales, with PCE, male sex, and other covariates.
Results: Higher PM levels, as measured by caregiver report, predicted EACE for early adolescent females ($p<0.05$), but not for males ($p>0.05$), with PCE and other covariates held constant. This was not the case when the early adolescents reported on PM.
Conclusions: EACE assessment via bioassay, and not by child or parent report, is a strength and lends credence to the observed association. It is possible to speculate that the relationship is predictive and not merely correlational, but firm conclusions cannot be drawn about cause-effect relations.
Financial Support: ORWH/NIDA P50 DA 024584; NIDA R01 DA 006556, K01 DA 016720, K05DA15799

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TRANSITION FROM USING OPIOIDS TO METHAMPHETAMINE AMONG FEMALES: A REPORT FROM A RESIDENTIAL DETOXIFICATION CENTER.

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Aims: The transition from using opioids to methamphetamine (MA) use is an emerging health problem among some Iranian females which could result in crucial health concerns. Yet, the underlying reasons associated with this transition are unknown.
Methods: In 2011-2012, a cross-sectional survey was conducted at the largest female residential detoxification center in Iran to explore the prevalence and reasons associated with transition from using opioids to MA among clients. All clients (n=500) were recruited and interviewed using a semi-structured questionnaire. Data was analyzed by performing descriptive statistics and the Chi-square test in SPSS (version 18)
Results: The mean age of the respondents was 31.8 (SD= 8.5) years. Half of the clients were married (51.8%), while fewer were separated and/or divorced (26.2%). Opioids were initial drugs of use. At admission, 30.2% had experienced transition to coadministration of MA with other drugs and 30% were MA users while the remaining clients were still users of opioids. 1.6% reported injecting opioids. Mean length of dependence on MA use was 4 (SD=4.5) years. Initial reasons associated with transiting from using opioids to MA included experience-seeking (61%), lack of definite plans for daily life and leisure (55%), social and family networks (49%), reducing depressant effects of opioids (43%), and peer group conformity (33%). MA users were younger, had initiated drug use earlier, and reported more risky sex compared with users of opioids.
Conclusions: Transiting from using opioids to MA could have important clinical and treatment implications for some Iranian females and the reasons associated with this problem should be considered in designing and implementing drug education and prevention programs for this group.
Financial Support: No financial support was received.

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SEX DIFFERENCES AMONG OPIOID-ABUSING CHRONIC PAIN PATIENTS IN A CLINICAL TRIAL.

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Aims: The characteristics of patients with co-occurring chronic pain and prescription opioid abuse have not been well described, and even less is known of differences between men and women in this population. The aim of this study was to evaluate sex differences in the demographic, diagnostic, and behavioral attributes of patients with chronic pain and opioid abuse.
Methods: Data were collected from 187 patients (139 M, 48 W) who screened for a study investigating the abuse liability of prescription opioids under sl buprenorphine/naloxone maintenance. Data were collected via self-report and semi-structured clinical interviews.
Results: The sample was primarily black (40%) and white (38%), with an average age of 46.8 (± 9.3) years. The majority of participants (90%) had chronic musculoskeletal pain in addition to opioid dependence. Participants had used prescription opioids for a mean duration of 5.4 (± 6.7) years. No significant sex differences were observed in types of pain, ethnicity, age and years of prescription opioid use. Women reported a greater severity of worst pain in the last 24 hrs (M=8.32/10, SD=1.64) compared to men (M=7.8/10, SD=1.72), $t(169)=-1.82$, $p=.091$. Pain had a greater effect in women (vs. men) on mood, walking ability, social relations ($p<.05$); general activity and sleep ($p<.1$). More men reported abuse of alcohol or illicit drugs, unauthorized dose increases, contact with street culture, being arrested by police, and were increasingly unkempt or impaired. Women were more depressed (M=17.7, SD=9.2) than men (M=14.0, SD=7.6), $t(81)=-1.82$, $p=.07$, on the Hamilton Depression scale.
Conclusions: The demographic profile of opioid-abusing chronic pain patients presenting for treatment in a clinical trial was similar between sexes. However, women reported more psychiatric co-morbidity, higher levels of worst pain, and greater pain-related physical and social impairment. Men reported more alcohol/drug use, contact with street culture, and arrests, and were more likely to increase dose without authorization.
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BDNF LEVELS AT UMBILICAL CORD BLOOD (UCB) AMONG BABIES EXPOSED TO CRACK DURING PREGNANCY.

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Aims: Background - Crack use during pregancy is a major health concern, since this substance may be toxic to the body on both a systemic and cerebral systems. It is believed that Brain-Derived Neurotrophic Factor (BDNF) may be involved in mediating the process of adaptation to chronic stress, including substance abuse disorder. Not much is known of the behavior of this variable in umbilical cord blood of babies whose mothers used crack during the pregnancy.
Methods: It is a study of a series of cases, where serum concentrations of BDNF levels at UCB among babies exposed to crack uring pregnancy where compared to non-exposed babies. The sample of non-exposed babies' stems was derived by mothers who accepted to donate the cord blood of their babies to Bank Umbilical Cord Blood and Placenta of our institution. The levels of BDNF were measured in UBC. The study factor is being a baby exposed to crack during pregnancy and the main outcome measure is the BDNF level at UBC.
Results: The sample was comprised by 27 infants whose mothers smoked crack during pregnancy and by 26 infants from healthy mothers. BDNF levels at UBC were significantly higher among babies exposed to crack during pregnancy (median = 22.34) in comparison to non-exposed babies (median = 9.58. Mann-Whitney $U = 199$, $Z=-2.704$, $p=0.007$, $r= -0.375$.).
Conclusions: Probably, the crack consumption of the mother reaches the baby brain, causing damages and modifications in synaptic connections and plasticity, with consequences on neurotransmission system. Therefore, there would be a process of adaptive increase of BDNF in order to seek a neuronal survival.
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EVALUATING A RAPIDLY EXPANDING METHADONE SYSTEM IN CHINA.

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Aims: To characterize methadone maintenance treatment (MMT) episodes among patients in one of the world's newest, largest and most rapidly expanding methadone systems in Wuhan, China.
Methods: Utilizing routinely collected data from the Chinese Centers for Disease Control, we evaluated baseline and treatment data, number of treatment episodes in 2010 (from first dose in 2010 until missing 30 consecutive days), the average/modal maximum prescribed daily dose, and average daily equivalent dose received (total dose received per patient/number of days of treatment episode) for 8811 patients who had at least one dose of methadone in one of Wuhan's 20 MMT programs in 2010. For patients who had one or more new treatment episodes during 2010, we calculated initial methadone dose for new treatment episodes.
Results: Over 1.3 million doses of methadone were administered to 8811 patients. Patient characteristics at entry: mean age 41 years (SD 7.3); 70.6% male; 43.3% married; 73.2% live with family; 69.8% with 'middle school' or less education; modal age of first drug use 28 (SD 7.4) and mean duration of drug use 13.2 years (SD 5.5); 62.5% had injection drug use in the past month. 74% were HCV positive and 0.28% were HIV positive. 83% had only 1 treatment episode in 2010, 12.2% had 2 and 1.3% had 4 or more episodes within the year (range 1-7 episodes); 7% of treatment episodes lasted only one day. The modal maximum dose was 80 mg of methadone per day, with the mean maximum dose of 77 mg (range 5 mg – 235 mg), and daily equivalent dose per treatment episode was 39.6 mg methadone (SD 24.1). For those who had a new treatment episode in 2010 (1475/8811), the mean starting dose for a new treatment episode was 65.5 mg (SD 25.8).
Conclusions: The rapid expansion of MMT in China has attracted a large number of admissions, but provision of safe and effective methadone dosages and optimizing treatment outcomes (e.g., retention) are identified as priority areas for improving treatment.
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GAZE TIME AS A SENSITIVE MEASURE OF COCAINE-RELATED ATTENTIONAL BIAS.

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Aims: Attentional bias to drug-related stimuli, measured by response time, has been demonstrated in abusers of a variety of substances. Evidence suggests that gaze time is a more direct measure of attentional bias than response time, however gaze time to cocaine-related stimuli has not been well explored. We hypothesized that cocaine users would show an attentional bias to cocaine-related stimuli as measured by response time and gaze time to the visual probe, and that gaze time would be a more sensitive measure of attentional bias.
Methods: Fourteen human subjects with histories of recent cocaine use completed a visual probe task with eye-tracking technology during two outpatient sessions. Subjects were presented with a series of side-by-side images that contained cocaine-related or neutral images. Eye-tracking technology measured time spent gazing at each image. A probe then replaced one image and time to respond was measured. Attentional bias scores were defined as the difference between neutral and cocaine-related images for gaze time and response time. Data were analyzed with repeated measures ANOVA and linear regression.
Results: Subjects demonstrated a large attentional bias to cocaine-related images relative to neutral images as measured by gaze time, which remained stable across both sessions. Subjects did not demonstrate an attentional bias as measured by response time. Gaze time correlated with cocaine use variables but not response time.
Conclusions: These data demonstrate that cocaine-related stimuli elicit a strong attentional bias in cocaine users and that gaze time, but not reaction time, is sensitive to this effect. Gaze time as a measure of attentional bias may be useful as a behavioral marker of drug use or as a target of drug treatment. Future research should determine specificity by including other control conditions and examine how attentional bias may be manipulated.
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AN EXPERIMENTAL TRIAL OF ADAPTIVE PROGRAMMING IN DRUG COURT: LONG-TERM OUTCOMES.

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Aims: Studies in drug courts reported improved outcomes when participants were matched at baseline to schedules of judicial status hearings based on their criminological risk level. This study examined the incremental efficacy of periodically adjusting the schedule of status hearings and clinical case-management sessions in response to participants' performance in the program. Initial findings showed the adaptive intervention to be more than twice as effect than baseline-matching-only in improving abstinence during the first 18 weeks of enrollment (Marlowe et al., 2012). The current analyses seek to determine whether these effects persisted following program completion.
Methods: In the initial study, 125 misdemeanor drug court clients were randomly assigned to an adaptive or baseline-matching condition. All participants were scheduled to attend bi-weekly status hearings if they were high risk or as-needed hearings if they were low risk. In the adaptive condition, participants were assessed at monthly intervals to determine how they were progressing in the program, and status hearings or case-management sessions were increased pursuant to the adaptive algorithm. For the current analyses, we examined between-group differences on arrest rates (18 months post-entry) and urinalysis results and psychosocial problems at the 6 and 12-month follow-up appointment.
Results: Between-group differences in arrest rates, urinalysis results, and psychosocial problems were small and non-significant. 22 percent of study participants were re-arrested for at least one new offense at 18 months. Most were for misdemeanor offenses and about half were for drug-related offenses.
Conclusions: Future research should evaluate adaptive algorithms that taper down the provision of services over time and employ other continuing-care strategies in an effort to prepare offenders for long-term maintenance of drug abstinence and desistence from crime.
Financial Support: R01-DA-013096

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CONTRACEPTION CONTINUATION AMONG FEMALE EXOTIC DANCERS SEEKING MOBILE REPRODUCTIVE HEALTH SERVICES CONCURRENT WITH SYRINGE EXCHANGE.

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Aims: Female exotic dancers are an understudied population with a high prevalence of drug and alcohol use, risk factors for transactional sex and inconsistent condom use. In 2009, the Baltimore City Health Department expanded their mobile syringe exchange program to include reproductive health services in the "Red Light" district. The objective of this study was to describe depot medroxyprogesterone acetate (Depo-Provera) continuation patterns among female exotic dancers seeking these mobile health services.
Methods: We performed a retrospective analysis of 75 clients who initiated Depo-Provera at a mobile health clinic attached to a syringe exchange from November 2009 to August 2012. Demographics, Depo-Provera uptake and continuation over 12 months were assessed by chart review. Characteristics between clients who continued Depo-Provera at 3 months and those who did not were compared using chi-square and t-tests.
Results: Seventy-two percent (N=52) of clients were African American, and 62% (N=42) were 24 years or younger. At 3 months, 36% (N=25) continued Depo-Provera. Clients who were Caucasian ($p=0.03$) and received other reproductive health services ($p<0.01$) were more likely to continue. At 6 and 12 months, 29% and 7% of all clients who initiated Depo-Provera continued, while successive continuation rates for those receiving the previous injection were higher at 54% and 63%.
Conclusions: Continuation of Depo-Provera among female exotic dancers is similar to that of the general population, with low overall but higher successive continuation after 3 months. Our study illustrates that integrating mobile reproductive health services into a needle exchange program can help fulfill the unique health needs of this high-risk population.
Financial Support: None.

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Δ⁹-TETRAHYDROCANNABINOL DOES NOT SUBSTITUTE IN RATS TRAINED TO SELF-ADMINISTER WIN55212-2.

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Aims: Although THC i.v. self-administration has been demonstrated in nonhuman primates, establishing THC self-administration in rodents has proven difficult. In contrast, self-administration of a synthetic cannabinoid, WIN55212-2 (WIN), in rats has been reported. The purpose of this study was to examine if rats trained to self-administer WIN would also self-administer THC.
Methods: Male Long-Evans rats were trained to self-administer cocaine (COC; 0.03 mg/kg/infusion) or WIN (0.01 mg/kg/infusion) through autoshaping. Rats were then maintained on a fixed ratio 3, with 3 priming infusions given at the beginning of each 3hr session. Dose-effect curves of the training drugs were assessed followed by pretreatment with rimonabant. Dose-effect curves were then determined for WIN in the COC group, and THC in the WIN group.
Results: Rats self-administered COC and WIN at levels significantly above vehicle. Rimonabant decreased responding for both drugs. When WIN was substituted for COC, rats did not acquire self-administration of WIN. Similarly when THC was substituted for WIN, rats did not acquire self-administration of THC.
Conclusions: The methods used here produced similar amounts of WIN intake compared to previous studies in rats; however, THC did not substitute for WIN. Between subject variability was high for both WIN and THC. Given the typical within class substitution observed in previous self-administration studies, these results suggest that the reinforcing effects of WIN and THC differ in rats. In previous research, establishing self-administration of other drug classes (e.g. stimulants) has also been largely unsuccessful in producing THC self-administration. Similarly, in the present study rats with a history of COC self-administration did not self-administer WIN, suggesting that exposure to a more reinforcing drug may decrease the likelihood of self-administration of cannabinoids, or that substitution across drug classes is not a reliable method for assessing abuse liability for cannabinoids.
Financial Support: RTI International internal research and development funds and NIDA Grants DA-03672 and DA-031988

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HAIR CORTISOL AS A BIOMARKER OF STRESS IN COCAINE-EXCITED DELIRIUM.

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Aims: The term Excited Delirium Syndrome (ExDS) has traditionally been used in the forensic literature to describe a subgroup of patients with delirium who suffered lethal consequences from their untreated severe agitation. Although the exact signs and symptoms are difficult to define precisely, clinical findings often include tolerance to significant pain, rapid breathing, sweating, severe agitation, elevated temperature, delirium, non-compliance or poor awareness to direction from police or medical personnel, lack of fatiguing, unusual or "superhuman strength", and inappropriate clothing for the current environment. Individuals displaying ExDS are at high risk for sudden death and therefore ExDS represents a true medical emergency. Cortisol is the canonical stress hormone and elevated cortisol level and stress sensitivity have been positively correlated with increased cocaine consumption. Hair cortisol incorporation reflects a general average cortisol level for a duration of time before sampling and allows a retrospective quantitative stress assessment.
Methods: We hypothesized that cortisol levels would be significantly elevated in cocaine-related ExDS, since cocaine abusers are at risk for developing ExDS. We extracted cortisol from hair and measured unit cortisol concentration (pg/mg) using the enzyme-linked immunosorbent assay (ELISA) method from age-matched controls (n = 38), chronic cocaine abusers (COC, n = 34), and cocaine-related delirium (ExDS, n = 34).
Results: There was a two-fold increase in cortisol levels in cocaine abusers compared to control subjects. In ExDS subjects, there was a four-fold increase in hair cortisol compared to controls ($p < 0.001$).
Conclusions: Stress induces changes in higher nervous system/sleep wakefulness, fear, autonomic function and activation of the HPA axis. Elevated hair cortisol levels suggest that in chronic cocaine abuses, stress may contribute to the pathophysiology of ExDS.
Financial Support: Supported by NIDA grant DA06227-19

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BINGE ALCOHOL CONSUMPTION IN EMERGING ADULTS: ALTERED ANTERIOR CINGULATE CORTICAL THICKNESS IS ASSOCIATED WITH ALCOHOL USE CONSEQUENCES.

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Aims: The brain undergoes dynamic and requisite changes into the early twenties that are associated with improved cognitive efficiency, particularly in prefrontal regions. As alcohol consumption is typically initiated and progresses to binge drinking during this time, the current objective was to investigate the impact of binge alcohol consumption on frontal lobe cortical thickness in emerging adults.
Methods: 10 binge drinking (BD; 3 males, mean age 22.0 ± 1.0) and 13 light drinking (LD; 5 males, mean age 21.7 ± 2.0) emerging adults underwent high-resolution magnetic resonance imaging at 3 Tesla. Cortical surface reconstruction and thickness estimation were performed using Freesurfer to examine bilateral anterior cingulate cortex (ACC), posterior cingulate cortex (PCC) and parieto-occipital sulcus (POS) cortical thickness estimates. The Young Adult Alcohol Consequences Questionnaire (YAACQ) was used to assess consequences associated with binge and light drinking.
Results: Cortical thickness was significantly lower in BD than LD in the right midACC (mACC; $p<0.005$). Lower cortical thickness also trended towards significance in the left dorsal PCC (dPCC; $p=0.06$) and left POS ($p=0.06$). Thinner mACC correlated with higher quantity and frequency of drinks consumed ($p<0.05$), and with greater impaired control over drinking and negative self-perception, self-care neglect, and greater risky behaviors (YAACQ, $p<0.05$).
Conclusions: Findings suggest that intermittent heavy alcohol consumption and alcohol-related negative consequences are associated with cortical thinning of the right mACC in emerging adults, with additional trends towards thinning of the left dPCC and POS. Binge drinking during emerging adulthood may therefore interfere with the finalization of neuromaturational processes via microarchitectural thinning.
Financial Support: K01AA014651 and R01AA018153 (MMS)

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RISK AND PROTECTIVE FACTORS OF TRANSACTIONAL SEX INVOLVEMENT AMONG SUBSTANCE USING ADOLESCENTS IN AN URBAN EMERGENCY ROOM (ED).

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Aims: Substance abuse (SA) and transactional sex (TS) involvement are highly correlated behaviors, with the average age of initiation of both SA and TS occurring in adolescence. Yet, reports of prevalence and correlates of these co-occurring behaviors among adolescents are sparse. The current study aims to evaluate the risk and protective factors of youth who report recent substance use and TS involvement.
Methods: A total of 600 youth ages 14-24 who reported drug use within the past 6 months were recruited from an urban ED, as part of a larger study. Participants were asked about the following risk/protective factors – substance abuse, mental health, sexual risk behaviors including TS, relational and community violence, parental substance abuse and parental support, positive and negative peer influence, fighting self-efficacy, healthcare utilization, and community involvement.
Results: Of the sample, 7.3% reported involvement in TS within the past month. Bivariate analyses indicated that youth who reported TS involvement, as compared to youth with no TS involvement, reported higher rates of the following risk factors - more than one sexual partner, intimate-partner, family, and community violence, and more severe mental health problems. Substance abuse indicators and all protective factors were non-significant.
Conclusions: Youth who report recent TS involvement are more likely to report experiencing increased mental health problems and violence as compared to other youth. Substance abuse was non-significant, suggesting that other risk factors should be considered when evaluating the relationship between substance abuse and TS involvement.
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ENHANCEMENT OF BENZODIAZEPINES ON ABUSED DRUG-INDUCED HYPERLOCOMOTION.

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Aims: It has been well known that benzodiazepines relieve anxiety, sleep disturbance and epilepsia. It is also known that benzodiazepines are relatively safe compared with barbiturates, because of their fewer side effects. However, the long-term use of benzodiazepines can cause psychological and physical dependence. Psychological dependence is considered to be accompanied by the neuroplastic change in the dopaminergic system, which projects from the ventral tegmental area to the nucleus accumbens, underlying mechanisms of drug dependence induced by benzodiazepines is not fully understood. Previously, we found that neuroplastic change based on alteration of KCC2 levels in the nucleus accumbens by chronic treatment with benzodiazepines enhanced morphine-induced hyperlocomotion. To confirm our previous finding, we examined the effects of chronic treatment with benzodiazepines induced neuroplastic change in the nucleus accumbens on the methamphetamine-induced hyperlocomotion in mice.
Methods: Locomotor activity by titling type cage was automatically recorded for 30 min prior injection and for 180 min after methamphetamine (1 mg/kg s.c.) administration. Diazepam (10 mg/kg i.p.) was administered once a day for 7 days before methamphetamine injection.
Results: We previously found that KCC2 protein level is increased by chronic treatment with zolpidem in the nucleus accumbens ($F(3,24) = 6.400$, $p<0.01$). Chronic treatment with diazepam significantly enhanced methamphetamine-induced hyperlocomotion, suggesting that chronic treatment with benzodiazepines can cause a neuroplastic change in the nucleus accumbens.
Conclusions: Chronic treatment with benzodiazepines can easily activate mesolimbic dopaminergic system. Furthermore, chronic treatment with benzodiazepines induces neuroplastic change in the nucleus accumbens, and such change regulated by KCC2 may influence the dopamine-related behavior as a postsynaptic event.
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BODY MASS INDEX (BMI) AND OBESITY PREVALENCE AMONG SUBSTANCE ABUSE PARTICIPANTS FROM NIDA'S CLINICAL TRIALS NETWORK.

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Aims: Though behavioral and pathological similarities between binge eating disorder and substance use disorders are known to researchers, associations between them are poorly studied. We compared pre-treatment BMI in substance users from 7 NIDA CTN clinical trials with that for age, race and gender comparable participants from the National Health and Nutrition Examination Survey (NHANES).
Methods: Standardized Prevalence Ratio (SPR) of obesity (BMI≥30kg/m^2) was estimated and adjusted for age, gender, and race. ANOVA test was used to compare adjusted mean BMI. Cigarette smoking status was also adjusted for in a subset of participants with available data.
Results: CTN participants had lower BMI (N=2017, mean=26.6kg/m^2) than NHANES participants (N=10966, mean=28.6kg/m^2, $p<0.0001$). Crude obesity prevalence was 23% and 37% in CTN and NHANES participants, respectively. Adjusted obesity prevalence in CTN participants was 32% lower than NHANES (SPR=0.68, 95% CI: 0.62-0.74). Obesity prevalence in NHANES participants was 2.75 times that in CTN opiate users (N=908, SPR=2.75, 95% CI: 2.27-3.38), but only 1.21 times that in CTN stimulant users (N=1109, SPR=1.21, 95% CI: 1.09-1.34). After further adjusting for smoking, obesity prevalence in CTN stimulant users was not different from NHANES participants (SPR=0.99, 95% CI: 0.90-1.10). BMI for CTN opiate users (mean=25.1kg/m^2) was lower than for stimulant users (mean=28.2kg/m^2, $p<0.001$), while obesity prevalence in stimulant users was 2.54 times that in opiate users (SPR=2.54, 95% CI: 2.29-2.81).
Conclusions: Obesity prevalence was significantly lower in substance abusers from CTN trials than in a matched sample of general population. The difference was driven by significantly lower BMI and obesity prevalence in opiate than stimulant users, suggesting substance-specific effects on energy homeostasis and weight regulation. Our results warrant further research on relationships between substance use, diet and weight.
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CONTEXT OF EARLY ADOLESCENT ALCOHOL USE: FIRST RESULTS FROM A LONGITUDINAL COHORT.

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Aims: Alcohol is one of the leading contributors to the burden of disease in young people. Despite this, little is known about the context of adolescent alcohol initiation and the development of harmful drinking trajectories. This research reports baseline data from an Australian longitudinal cohort.
Methods: A total of 1,977 parent-child dyads were recruited Australian secondary schools. During 2010/11, 1,929 parent-child dyads completed baseline surveys. Measures include: alcohol use and harms; rules; parental style and monitoring; family relationships and conflict; peer substance use and approval; and delinquency.
Results: Sixty-eight percent of adolescents reported lifetime alcohol involvement. Adolescent alcohol initiation was associated with parent factors: frequency and quantity of alcohol use ($\chi2(3, N=1880)=79.3$, $p<0.000$; $\chi2(3, N=1879)=63.8$, $p<0.000$), drinking alcohol in the presence of their child ($\chi2(3, N=1879)=81.63$, $p<.000$) and younger age of parent alcohol initiation ($\chi2(1, N=1785)=20.1$, $p<0.000$). Adolescents more likely to try alcohol reported: higher levels of rule breaking and aggressive behaviour ($\chi2(1, N=1903)=44.4$, $p<0.000$; $\chi2(1, N=1893)=13.4$, $p=0.000$), being male ($\chi2(1, N=1904)=6.7$, $p=0.010$), and having substance-using ($\chi2(3, N=1896)=506.9$, $p<0.000$) and approving ($\chi2(2, N=1903)=91.2$, $P<0.000$) peers.
Conclusions: Context of adolescent alcohol initiation and use provides important insight into understanding the nature of alcohol use and misuse . Given alcohol involvement often commences during this developmental period, understanding how different initiation and consumption contexts shape different trajectories may play an important role in future screening and prevention efforts. This in turn can inform international alcohol policy, as well as communities and families.
Financial Support: Australian Research Council
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CONTINGENCY MANAGEMENT INTERVENTION TAILORED FOR JUVENILES IN DRUG COURT: PRELIMINARY SHORT-TERM SUBSTANCE USE OUTCOMES OF A RANDOMIZED CONTROLLED TRIAL.

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Aims: The aim of this study was to assess short-term substance use outcomes of an ongoing randomized controlled trial (RCT) of a contingency management (CM) and sexual risk reduction intervention for juveniles in drug court. We hypothesized that abstinence, defined as having all negative urine drug screens (UDS) during the 6-month intervention period, would be higher in the CM arm than usual services (US).
Methods: Participants were recruited from two drug courts with parental and youth informed consent. The present study included 72 youth who completed at least 6 months of the RCT (CM=32, US=40). UDS were collected at baseline (BL), 3-months, and 6-months; missed UDS were considered positive (5.5%). Chi-squared tests were used to detect BL between-group differences. Multivariable logistic regression was used to calculate the relative odds of abstinence (no positive UDS) by 6 months post-BL comparing CM to US, adjusting for BL number of substances ever used.
Results: Participants had a mean age of 15.1 (SD=0.15); 85% were male, 50% white, 36% black, and 35% Hispanic. There were no demographic group differences; 40.6% of CM and 27.5% of US had a positive UDS at BL ($\chi2=1.38$, $p=0.24$). The adjusted odds of abstinence by 6 months post-BL for CM youth was 2.37 times that of US, though not statistically significant (95% CI=0.59-9.88, $p=0.24$). With each additional substance ever used at BL, there was a significant 31% reduction in odds of abstinence (95% CI=0.51-0.93, $p=0.016$).
Conclusions: Although there was a trend of positive intervention effects, there was no statistical difference in abstinence comparing CM to US by 6 months post-BL. Given the limited sample and short follow-up, additional research is planned to assess the long-term outcomes of the intervention.
Financial Support: This study was supported by grants R01DA025880 and T32DA007292 from the National Institute on Drug Abuse.

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CANNABIS AND ALCOHOL: IS THERE A RELATIONSHIP FOR DRIVERS?

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Aims: The 2007 National Roadside Survey identified cannabis as the most frequently identified drug found in the drivers, and of those individuals who entered Texas publicly-funded programs with at least one past-year DUI, 66% (22,666) had a primary problem with alcohol and 13% (4,438) had a primary problem with cannabis. The aim of this paper is to examine the characteristics of these drivers at treatment admission who were primarily cannabis users as compared to those using cannabis and alcohol and those with a primary problem with alcohol.
Methods: A database of 56,717 treatment admissions of DUI drivers was examined using correlation and significance tests to determine differences in these individuals and to assess their risks for abstinence after completing treatment
Results: Individuals with a problem with cannabis but no alcohol problems were younger had used their primary drug fewer years, were less likely to complete treatment, had lower income, had fewer substance abuse problems, and were more likely to be homeless, as well as more likely to be Hispanic. Those who only had problems with alcohol were older, had been in treatment more times, had used more years, had more severe levels of impairment, but completed treatment and had higher incomes. Between these two extremes were those who had primary problems with cannabis and secondary with alcohol and those who had primary problems with alcohol and secondary with cannabis. As their problems with alcohol grew and problems with cannabis decreased, their severity increased in terms of ASI problems, employment, need for medications, emergency room visits, and non-DUI arrests.
Conclusions: Impaired drivers who first develop problems with cannabis appear to move along a continuum that includes adding alcohol as the second problem, then developing more problems with alcohol and less with cannabis, and finally having serious problems with alcohol. Use of these two drugs in various combinations of intensity is a factor that should be to lessen driving under the influence.
Financial Support: None

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CURRENT AND FORMER METHAMPHETAMINE-DEPENDENT ADULTS SHOW ATTENUATED BRAIN RESPONSE TO PLEASANT INTEROCEPTIVE STIMULI.

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Aims: MD and AB individuals will show a diminished response to interoceptive stimuli.
Methods: Recently abstinent MD (n=25), long-term AB (n=17), and comparison (CO, n=17) subjects completed a continuous performance task during functional magnetic resonance imaging while receiving a pleasant interoceptive stimulus. During anticipatory trials, a blue or yellow background signaled an impending slow brush stroke administered to the left palm or forearm, respectively, during upcoming interoceptive trials. Visual analog scales (VAS) indexed interoceptive experience (e.g. pleasantness, intensity). A linear mixed effects model was conducted with group as the between subjects variable, subject as a random factor, and condition (anticipation palm and forearm, soft touch palm and forearm) as the repeated factor. Correlations between significant brain results and VAS ratings were computed.
Results: CO exhibited greater left posterior insula activation than MD and AB across trials. CO also showed greater activation than MD and AB in bilateral anterior cingulate and dorsal striatum during soft touch. Despite striatum attenuation during soft touch, AB rated the soft touch as more pleasant and less intense than MD and CO who did not differ.
Conclusions: MD and AB exhibit attenuated interoceptive processing and decreased reward responsivity, findings that may relate to a reduced sensitivity to pleasant stimuli. Self-report and brain indices of reward may recover at different rates with long term abstinence from stimulants.
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RELIABILITY AND VALIDITY OF A SUBSTANCE CRAVING SCALE.

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Aims: Substance craving scales in the current literature are limited in both their scope and the sophistication of their conceptual development. It is suggested that dimensions of craving may be more general, rather than substance specific. The aim of this research is to develop a substance craving scale that is reliable and valid for use across substance use disorders. The research will examine via the Rasch model the reliability and validity of the scale, which was developed for use across substances, individuals, and treatment settings.
Methods: Data were collected from 1,043 adults who had presented to publicly funded substance abuse treatment between 1996 and 1998 and are being followed for 18 years as part of the Pathways to Recovery (Scott et al 2011) study. The participants were 89% African American, 4% Caucasian, 6% Hispanic, and .2% other and 62% female. In the year prior to the interview, 33% where in recovery and 37% using (27% cocaine, 27% opioids, 23% heavy alcohol,21% cannabis).
Results: Only 1 of 12 items exhibited item misfit using the criterion of >1.33 for both Infit MNSQ and Outfit MNSQ. After removing one misfitting item, the craving scale was found to (a) be unidimensional, (b) have a hierarchical severity structure, and (c) met hypothesized correlations with criterion variables. The scales was judged to be unidimensional using the proportionality criterion of a 4 to 1 ratio for the variance explained by the principal measure to the variance explained by the first factor of residuals. Cronbach's alpha reliability was high at .92.
Conclusions: The craving scale was found to be unidimensional, have a hierarchical severity structure, and met hypothesized correlations with criterion variables. Moreover, the scale appears to work across people using different substances.
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NONMEDICAL USE OF PRESCRIPTION STIMULANTS TO HELP STUDY AMONG U.S. HIGH SCHOOL SENIORS.

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Aims: This study examines the motives for nonmedical use of prescription stimulants (NMUPS) among U.S. high school seniors and assesses associations between motives for nonmedical use and problem behaviors.
Methods: Data were collected via self-administered questionnaires from nationally representative samples of U.S. high school seniors (modal age 18) as part of the Monitoring the Future study. The sample consisted of 4,519 individuals (52% female) in senior year cohorts 2009 and 2010.
Results: Among those who reported past-year NMUPS (e.g., Adderall, Ritalin, Concerta), an estimated 3.3% (se = 1.2%) indicated "to help study" only, 35.5% (se = 3.9%) indicated "to help study" and other non-study motives (e.g., to get high), and 61.2% (se = 4.0%) indicated non-study motives only. The odds of binge drinking in the past two weeks (AOR = 6.7, 95% CI = 3.8 – 11.6), truancy in the past month (AOR = 3.3, 95% CI = 1.9 – 5.7), and a C+ GPA or lower (AOR = 3.0, 95% CI = 1.6 – 5.8) were significantly greater among high school seniors who reported past-year NMUPS "to help study" as compared to those who did not report past-year NMUPS. The students who reported NMUPS "to help me study" as their sole motive had the lowest mean GPA. Approximately 60% of those who reported NMUPS "to help study" engaged in binge drinking, truancy, and three or more evenings out for fun per week. There were minimal differences in problem behaviors between those who reported past-year NMUPS "to help study" as compared to those who reported past-year NMUPS for other non-study motives.
Conclusions: These findings suggest that NMUPS is significantly associated with problem behaviors regardless of motive, which has important implications for efforts to reduce NMUPS among adolescents.
Financial Support: Supported by NIDA research grants R01DA024678 and R01DA031160.

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THE MEDICATION RESEARCH PARTNERSHIP.

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Aims: The Medication Research Partnership seeks to a) accelerate medication-assisted treatment (MAT) for alcohol and opioid disorders, b) monitor health care utilization and cost, and c) assess barriers and facilitators to enhance the use of medication to treat alcohol and drug use disorders. The partnership includes a commercial health plan and 9 addiction treatment centers contracting with the health plan.
Methods: The partnership uses a systems change model emphasizing use of financial, regulatory, operational, inter-organizational, and customer impact levers, to implement organizational and system change projects that increase access to and use of medication-assisted treatment.
Results: Two treatment centers that streamlined intake processes reported a 52% increase in patients receiving medication and a 13% improvement in referrals from detox to outpatient. Two sites established criteria to assess patient appropriateness for MAT. Four sites developed medication treatment protocols. One site sought approval as an opioid treatment program. A second site increased patient adoption of extended-release naltrexone and are up to 2.5 injections per month. A third site increased the number and percent of patients prescribed extended-release naltrexone. The fourth site saw increased patient resistance to buprenorphine and increased interest in extended-release naltrexone. One site implemented physician training on MAT and increased the number of patients prescribed and receiving alcohol medications by 23%. The health plan provided case management assistance for patients using medication and encouraged treatment centers to prescribe medications.
Conclusions: Organizational change and systems change strategies can enhance the adoption of medication for treatment of alcohol and opioid dependence.
Financial Support: An award (R01 DA029716) from the National Institute on Drug Abuse supported the study

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TRAUMA HISTORIES OF NON-TREATMENT-SEEKING PRESCRIPTION OPIOID-DEPENDENT INDIVIDUALS.

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Aims: To describe the traumatic event histories of non-treatment seeking prescription opioid dependent (POD) individuals with respect to prevalence, gender differences and order of onset, and examine the relationship with motives for use and source of opioids.
Methods: Participants (N=99) met DSM-IV-TR criteria for current POD and were recruited from the community. Substance use disorders were assessed using the SCID, Time-Line Follow-Back, and Addictions Severity Index. Lifetime experience of events meeting the DSM-IV-TR definition of 'traumatic event' (TE) was assessed using the Life Stressor Checklist-Revised.
Results: The majority (86.9%) reported at least one TE. Initial TE occurred at an average age of 13.79 years, and exposure to multiple types of TEs was common (88.4%, M=4.30 TEs). No gender difference in prevalence of TE was observed; however, women experienced significantly more types of TEs than men (M=4.72 vs. 2.89; $p<0.01$). TE positive subjects were 5.44 times more likely than TE negative subjects to report a medical professional as their initial source. TE history did not differentiate between (medical versus non-medical) motive for initial use; however, TE negative subjects were significantly more likely than TE positive subjects to report non-medical reasons for current opioid use. With regard to order of onset, TE onset preceded first use and onset of POD for the majority of individuals (65.7% and 74.7%, respectively); however, men were 5.88 times more likely than women to report TE experience concurrent or subsequent to onset of POD (as opposed to preceding POD).
Conclusions: TE exposure is common among individuals with POD and typically precedes onset of POD, particularly among women. TE history is associated with differential initial sources and current motives for prescription opioid use. Findings support the integration of trauma and substance abuse screening and referral into routine prescribing practices.
Financial Support: This work was supported by NIDA grant K23 DA021228 (SEB).

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COST-EFFECTIVENESS ANALYSIS OF A RANDOMIZED TRIAL OF RECOVERY MANAGEMENT CHECKUPS FOR ADULTS WITH CHRONIC SUBSTANCE USE DISORDERS.

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Aims: To perform the first cost-effectiveness analysis (CEA) of RMC for adults with SUD
Methods: Incremental costs and effectiveness of a randomized clinical trial comparing RMC to a control group over a four-year follow-up period. Participants were recruited from the largest central intake unit for substance abuse treatment in Chicago, Illinois and randomly assigned to outcome monitoring (OM-only) or OM-plus-RMC with quarterly follow-up for 4 years. 446 participants who were 38 years old on average, 54 percent male, and predominantly African American (85%). Data on the quarterly cost per participant come from a previous study of OM and RMC intervention costs (Dennis et al., 2011). Two outcomes were selected for the CEA: days of abstinence and number of substance-use-related problems.
Results: Over the four-year trial, the average cost (per participant) of OM-plus-RMC was $4,889 compared to $2,705 for OM-only. Participants in OM-plus-RMC averaged 1,026 days abstinent and had 89.1 substance-use-related problems. OM-only averaged 932 days abstinent and reported 125.8 substance-use-related problems. Mean differences for both effectiveness measures were statistically significant ($p<0.01$). The incremental cost effectiveness ratio for OM-plus-RMC was $23.38 per day abstinent and $59.51 per reduced substance-related problem. When additional costs to society were factored into the analysis, the marginal cost of OM-plus-RMC dropped to $14.61 per day abstinent and $37.08 per reduced substance-related problem.
Conclusions: RMC is a relatively inexpensive intervention and, for any plausible willingness-to-pay assumptions, is a cost-effective strategy for promoting abstinence and reducing substance-use-related problems among chronic substance users.
Financial Support: Financial assistance for this study was provided by the National Institute on Drug Abuse (NIDA; grant numbers R37 DA011323 & R01 DA031785). ClinicalTrials.gov ID: NCT01153594

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MULTIPLE SCHEDULES AS A MODEL TO TEST CUE EFFECTS OF DRUG AND NATURAL REINFORCERS.

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Aims: Repeated exposure to drugs of abuse causes long-term neural changes that alter the way an organism responds to rewards, including reward-associated stimuli. However, preclinical study of these neural changes occurs often in animals exposed only to the drug. As drug-induced neural adaptations also affect the way organisms respond to natural reinforcers and their associated cues, parsing out drug-specific neural adaptations requires models that expose the organism to drugs, natural reinforcers and their cues.
Methods: Separate groups of rats were trained to self-administer methamphetamine (METH) and food or cocaine (COC) and food using a multiple schedule of reinforcement. Rats were given access to drug (METH or COC) and food according to a fixed-ratio 5 schedule of reinforcement in separate components signaled by 2 different discriminative stimuli. Following stable responding within each component, animals underwent extinction training in the absence of either discriminative cue for 14 days. After extinction, rats were exposed non-contingently to each cue (drug and food) alone.
Results: Repeated-measures ANOVA indicated that animals responded significantly more on the drug lever during drug components and more on the food lever during food components. Additionally, responding on both levers decreased during extinction. When re-exposed to the discriminative stimuli alone, responding on the drug lever increased only when exposed to the drug stimulus, and responding on the food lever increased only when exposed to the food stimulus. Finally, when animals were sated on food pellets, responding during cue tests only decreased during food components, indicating cue specificity.
Conclusions: Collectively, these data suggest that multiple schedules of reinforcement can be used to shape specific responses to stimuli associated with drugs of abuse or a natural reinforcer within a single animal. This model could be used to help target drug-specific neural adaptations and help in the discovery of new drug-specific targets for pharmacotherapies of drug abuse.
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PROGRAMMABLE BIO-NANO-CHIPS FOR THE QUANTITATION OF DRUGS OF ABUSE IN ORAL FLUIDS.

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Aims: To develop, validate and apply Programmable Bio-Nano-Chips (p-BNCs) for the detection and measurement of drugs of abuse in oral fluids.
Methods: p-BNCs quantify soluble targets in complex biological matrices, using agarose bead sensors with a size-tunable network of nanometer-scale fibers, arrayed within an enclosed microchip.
Results: Unlike existing portable and laboratory-based drug detection systems, the in-development technology allows for the simultaneous detection and quantitation of multiple drugs in ~10 minutes. These mini test ensembles have been shown to exhibit outstanding analytical performance and are now clinically validated against the reference method of Liquid Chromatography Tandem Mass Spectroscopy. The chip-based tests allowed for the elucidation of the time-course of drugs in oral fluids: cocaine/benzoylecgonine, were measured (LODpractical and LOQpractical of 1.0 and 10.0 ng/mL, respectively) as early as 10 minutes and up to ~50 hours post IV infusion, while methamphetamine (LOD=6.2 ng/mL, LOQ=8.1 ng/mL) demonstrated clearing 4 hours post its administration.
Conclusions: In their final embodiment, p-BNCs will have the potential to be used as a screening tool for "drugged-drivers", at the police station, a remote laboratory and at the roadside or point of arrest. This methodology may be extended to other settings, including drug rehabilitation centers, emergency rooms, prisons, schools, and the work place.
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CONTINGENCY MANAGEMENT TARGETING PSYCHO-STIMULANT USE RESULTS IN SECONDARY DECREASES IN SMOKING FOR SEVERELY MENTALLY ILL ADULTS.

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Aims: To determine if a contingency management treatment targeting psycho-stimulant abstinence in adults with severe mental illnesses (i.e., schizophrenia spectrum, bipolar, major depressive disorders) is associated with reductions in smoking.
Methods: 176 individuals with SMI and psycho-stimulant dependence were assigned to receive 12-weeks of treatment-as-usual and either CM for psycho-stimulant abstinence or a non-contingent control condition. The smoking outcome examined was smoking-negative carbon monoxide (CO<7ppm) breath-tests that were gathered 3 times a week for 12-weeks. Generalized estimating equations were used to evaluate the impact of CM on smoking abstinence controlling for time and condition.
Results: Three-quarters (78%,n=137) of the sample were smokers, defined as ≥2 positive CO breath-samples during the study. Smokers who received CM for psycho-stimulant abstinence were 24% (OR=1.24, CI=1.08-1.42) more likely to submit a smoking-negative breath sample during treatment than non-contingent controls.
Conclusions: These preliminary data suggest that CM treatment of psycho-stimulant use has a moderate secondary effect on smoking. Additional research that validates this effect using more rigorous methodologies (e.g., cotinine urine tests, self-report) and attempts to maximize this potential treatment effect of CM on psycho-stimulant and smoking outcomes by combining CM for psycho-stimulant abstinence with evidence-based smoking interventions is needed.
Financial Support: This research was supported by grants from the National Institute on Drug Abuse, R01DA022476-01 (PI: R.K. Ries) and the National Institute on Alcohol Abuse and Alcoholism, R01AA020248-01A1 (PI: M.G. McDonell)

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CUE-INDUCED CRAVING IN PRESCRIPTION OPIOID AND HEROIN DEPENDENCE.

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Aims: As the proportion of individuals presenting to treatment for prescription opioids has increased, research has begun to identify differences between this population and heroin users. However, research on the nature of the differences between these populations is in early stages and little is known about whether basic findings in heroin dependence generalize to prescription opioid dependence. The present study evaluated differences in cue-induced craving in individuals with a diagnosis of opioid dependence presenting to inpatient treatment, including both prescription opioid and heroin users.
Methods: Participants with a primary diagnosis of opioid dependence (N = 28) were recruited from an inpatient alcohol and drug abuse treatment unit. Participants were administered opioid images (including heroin and prescription opioid images) on a computer screen and provided ratings of craving and stimulus salience on a scale (0-10) following each stimulus.
Results: The heroin dependent (HD) group reported significantly greater salience of ($p < .05$) and craving following ($p < .05$) heroin stimuli than the prescription opioid dependent (PD) group; there were no group differences in response to prescription opioid stimuli. When comparing salience and craving in response to the primary drug of abuse, the HD group reported significantly greater salience of and craving to heroin images than prescription opioid dependent participants reported in response to prescription opioid images (mean difference = 3.21 for salience, 3.16 for craving).
Conclusions: Differences in cue-reactivity between prescription opioid and heroin dependent patients has implications for both the study and treatment of opioid dependence. Results of this pilot trial indicate that cue salience is specific to the opioid of abuse and that cue-induced craving is higher among heroin relative to prescription opioid dependent inpatients.
Financial Support: Support for this project was provided in part by the Livingston Fellowship from Harvard Medical School awarded to Dr. McHugh.

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HIV-1 TAT PROTEIN EXPRESSION IN MOUSE BRAIN POTENTIATES ETHANOL REWARD AND REINSTATES EXTINGUISHED ETHANOL-SEEKING BEHAVIOR.

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Aims: Although the HIV-accessory protein Tat increases midbrain dopamine levels, the functional consequences of Tat exposure on the rewarding effects of, and craving for, ethanol are little known. Accordingly, we hypothesized that HIV-1 Tat expression in brain would potentiate the psychostimulant effects of ethanol and reinstate extinguished ethanol-seeking behavior.
Methods: Using the GT-tg bigenic mouse model, where brain-selective Tat expression is induced by activation of a doxycycline (Dox) promotor, we tested the effects of Tat on ethanol conditioned place preference (CPP) and ethanol consumption in the two-bottle choice task. Western blot analysis was used to verify Tat expression in mouse brain.
Results: In Western blot analysis, uninduced GT-tg bigenic and Dox-treated C57BL/6J mouse brains demonstrated minimal labeling with Tat antibody at molecular weights corresponding to Tat protein. In contrast, Tat antibody labeling significantly increased in an exposure-dependent manner in GT-tg bigenic mice treated with Dox. Although mice expressing Tat demonstrated saline-conditioned place preferences similar to uninduced littermates, Tat expression significantly increased ethanol-CPP 2.8-fold in a manner dependent on the magnitude of exposure to Tat protein. Moreover, subsequent expression of Tat protein resulted in the reinstatement of an extinguished ethanol-CPP in previously uninduced mice. The results of two-bottle choice testing will be discussed.
Conclusions: Overall, these data suggest that Tat expression in mouse brain potentiates the psychostimulant behavioral effects of ethanol, and also induces reinstatement of extinguished ethanol-seeking behavior. Moreover, these results support one underlying biological basis for the HIV-related increased motivation for reinforcing drugs.
Financial Support: Funding was provided by NIMH (MH085607 to JPM) and the State of Florida, Executive Office of the Governor's Office of Tourism, Trade, and Economic Development.

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IMPLEMENTING SCREENING AND BRIEF INTERVENTION IN PUBLIC SCHOOLS: FEASIBILITY AND PROOF OF CONCEPT.

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Aims: Screening, brief motivational counseling intervention and referral to treatment (SBIRT) has shown to be effective in reducing substance use and related harms among adolescents in clinical settings but it had not been adapted for use in schools. This translational research study aimed to a) develop a proof of concept, b) test the feasibility of conducting SBIRT in two urban New York schools, and c) examine the economic sustainability.
Methods: With the cooperation of the New York OSAS, licensed "health clinics" were created within these schools, equipped with a computer screening program and a trained substance abuse counselor. The computer presented a standard substance screening; provided tailored prevention information to the student and provided counselor guidance for an immediate, private Motivational Interviewing counseling session.
Results: In Spring 2012, 248 students were randomly approached to participate; 100% accepted the screening; 42% of them (n=105) reported substance use (vs. 28% reported in school-wide, anonymous survey). Importantly, 99% of positively screened students voluntarily accepted one motivational counseling session and 68% returned for additional counseling sessions. The SBIRT procedure did not interfere with academic activities.
Conclusions: The SBIRT was feasible to implement and attractive to students, teachers and administration. We believe the acceptance and participation was due the use of non-school personnel and the private, professional and confidential procedures employed. The data offer clear indication that further effectiveness testing is warranted and potentially valuable.
SBIRT, as implemented, has been approved for Medicaid (and some private insurance) reimbursement without co-payment to the parents or students. Economic modeling demonstrates the current national SBIRT reimbursement rates to be adequate to broadly implement and sustain school-based SBIRT in most mid to large-sized schools.
Financial Support: Phoenix House and Treatment Research Institute

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PATTERNS OF INTERNET DISCUSSION ASSOCIATED WITH THE RELEASE OF ABUSE-DETERRENT FORMULATIONS OF PRESCRIPTION OPIOIDS.

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Aims: To evaluate levels and characterize patterns of Internet discussion before and after the release of two abuse deterrent formulation (ADF) opioids: reformulated OxyContin® and reformulated Opana® ER.
Methods: Utilizing NAVIPPRO®'s Internet Monitoring data stream, 5,919,531 posts from seven recreational drug abuse sites were collected from January 1, 2008 to September 30, 2012. Discussion levels for opioid compounds (oxycodone, oxymorphone, hydrocodone, buprenorphine, methadone, and morphine) and products (OxyContin, Opana ER, Roxicodone, Vicodin, and MS Contin) were quantified during the periods before and after the release of reformulated OxyContin and reformulated Opana ER. In addition, 2,400 randomly selected posts related to OxyContin and Opana ER (600 pre- and post-reformulation for each drug) were qualitatively reviewed and evaluated for discussion related to routes of administration, extraction, procurement, negative consequences, and general discussion.
Results: Little change was observed after the reformulation of OxyContin in levels of Internet discussion related to the compounds evaluated; however, at the product level a significant decrease was observed in the proportion of discussion related to OxyContin following the product's reformulation ($R2 = .67$, $p = .007$). Opana ER discussion increased significantly prior to OxyContin's reformulation ($R2 = .76$, $p = .001$), while Roxicodone discussion increased significantly over the entire 19-quarter period ($R2 = .56$, $p < .001$). No changes were observed for Vicodin and MS Contin. Finally, similarities in discussion patterns of OxyContin and Opana ER were observed before and after the release of the ADF versions. Pre-post changes in topics discussed were also similar for these two ADFs.
Conclusions: Internet monitoring is a valuable approach for evaluation of sentiment changes and tampering methods among a sentinel population of recreational drug abusers. Changes in abuse related discussion can be observed quickly following variations in formulations and may follow particular patterns.
Financial Support: Inflexxion, Inc.

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TEST-RETEST RELIABILITY OF A COMPUTER SELF-ADMINISTERED SUBSTANCE USE BRIEF SCREEN FOR TOBACCO, ALCOHOL AND DRUG USE.

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Aims: A major impediment to implementation of substance use screening and brief interventions (SBI) in healthcare settings is the lack of an efficient yet precise screening instrument that is compatible with clinical workflows. As a first step toward addressing this need, we developed the Substance Use Brief Screen (SUBS); a 4-item screener for tobacco, unhealthy alcohol, and drug use that is short, self-administered, and could be easily integrated with electronic health records. This study assessed the instrument's test-retest reliability.
Methods: The SUBS was self-administered on touchscreen tablet computers. Participants were recruited consecutively in the waiting area of a large urban safety net primary care clinic. Eligibility criteria were: current clinic patient, English speaking, age 18-65. Participants were administered the SUBS at the initial visit, and asked to return 1-2 weeks later; those completing both study visits were included in the analysis. Agreement between responses at the first versus second administration was evaluated with the phi coefficient and McNemar's tests.
Results: Of the 61 participants, 89% completed both visits. Reported rates of past year use were 39% for tobacco, 65% for alcohol (4+ drinks/day), and 50% for other drugs (including illicits and nonmedical use of prescription drugs). SUBS responses were 100% complete. Correlation between screening results on the first and second administration was excellent for tobacco (phi=.96) and drugs (phi=.78), and good for alcohol (phi=.63). There were no significant differences between administrations in detecting use, based on McNemar's tests, for any substance.
Conclusions: The Substance Use Brief Screen (SUBS) facilitated reporting of high rates of substance use, had good test-retest reliability, and was feasible in this sample of primary care patients. Further research is needed to evaluate the validity of the SUBS for detecting unhealthy use and substance use disorders.
Financial Support: NIDA K23 DA030395
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REWARDING EFFECTS OF SYNTHETIC CATHINONES.

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Aims: The increased use and abuse of synthetic cathinones calls for information concerning the abuse liability of these drugs. Using the conditioned place preference paradigm, this study examines which synthetic cathinones produced reward and therefore have the potential to maintain drug seeking.
Methods: 3,4-Methylenedioxypyrovalerone (MDPV), methylone, mephedrone, naphyrone, flephedrone, butylone, and pentylone were assessed for rewarding effects in the conditioned place preference behavioral assay. Four sessions each of drug or vehicle conditioning were presented. Doses were those which produced full substitution in drug-discrimination testing.
Results: MDPV (3 mg/kg), butylone (10 mg/kg), and pentylone (30 mg/kg) increased the amount of time spent on the drug-paired floor. Mephedrone (10 mg/kg), methylone (5 mg/kg) and naphyrone (5 mg/kg) produced apparent increases that did not reach statistical significance, whereas flephedrone (10 mg/kg) did not increase the time spent on the drug paired floor.
Conclusions: MDPV, butylone, and pentylone produced place preference, indicating that they induce reward, and have some potential for abuse. The remaining compounds did not produce strong preferences, although this may be due to non-ideal parameters for testing. Stronger place preferences may be observed at different doses or pretreatment times.
Financial Support: Supported by NIH N01DA-7-8872.

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GROWTH MIXTURE MODELING OF STIMULANT USE TREATMENT EFFECTS AND DIFFERENTIAL TRAJECTORIES: EVIDENCE FROM TWO CONTINGENCY MANAGEMENT CLINICAL TRIALS.

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Aims: This study examined the impact of contingency management (CM) on stimulant use heterogeneity across two 12-week clinical trials. We hypothesized that CM effects on stimulant use would differ across multiple sub-groups of patients with distinct trajectories of use throughout the treatment period.
Methods: Data for this study came from two National Drug Abuse Treatment Clinical Trials Network studies - 0006 and 0007 (N=832, Petry, et al. 2005; Peirce, et al. 2006). The outcome of positive stimulant urine analysis (UA+) was measured two times per week for 12 weeks. We used growth mixture modeling to estimate multiple latent class solutions (classes 1 through 6).
Results: The best fitting, clinically interpretable model was the 3-class linear model (BIC=7624). The model produced the following classes: Class 1 (21% of sample) = low probability (35%) of UA+ at baseline, steep decline in UA+ submissions during treatment, CM caused a large decline in UA+ submissions over time (β = -0.32, $p < 0.05$); Class 2 (38%) = moderate probability of UA+ at baseline (42%), moderate decline in UA+ submission over time, CM caused a moderate decline in UA+ submissions over time (β = -0.07, $p < 0.05$); Class 3 (41%) = high probability of UA+ at baseline (65%), increase in UA+ submissions over time and no effect of CM.
Conclusions: Identifying sub-groups may help explain heterogeneity in substance use trajectories and identify characteristics that could inform treatment non-response (e.g., Class 3). Such models could also assist with identifying segments of the stimulant use population who could benefit from ancillary services in order to more effectively impact abstinence.
Financial Support: Life Science Discovery Fund (Roll, PI), NIDA Clinical Trials Network Pacific Northwest Node (5 U10 DA013714-10; Donovan and Roll, Co-PIs), Washington State University Spokane Seed Grant Program (McPherson, PI).

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POLYDRUG USE AND RISK OF BLOOD-BORNE AND SEXUALLY TRANSMITTED INFECTIONS AMONG HEROIN IDUS IN TIJUANA, MEXICO.

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Aims: Although most injecting drug users (IDUs) in Tijuana primarily inject heroin, injection and non-injection use of meth and cocaine is common. We examined patterns of polydrug use among heroin injectors to inform prevention and treatment of drug use and its health and social consequences.
Methods: Participants were IDUs residing in Tijuana aged > 18 years who reported heroin injection in the past 6 months. Participants were recruited by respondent driven sampling and completed surveys and testing for HIV, TB, and syphilis (n=1025). Latent class analysis was conducted to assign individuals to classes on a probabilistic basis, using four indicators of past 6 month polydrug use: 1) cocaine injecting, 2) cocaine smoking or snorting, 3) meth injecting, 4) meth smoking or snorting. Chi-square tests and ANOVAs were used to detect differences between classes among categorical and continuous risk factors, respectively.
Results: Latent class analyses testing 1, 2, 3, and 4 classes were fit, with the 3-class solution fitting best. Based on conditional response probabilities, class 1 was defined primarily by high meth and cocaine use (6.0%, n=62), class 2 by high meth use (43.7%, n=448), and class 3 by a lack of polydrug use (50.2%, n=515). Significant differences ($p < .05$) between the 3 classes emerged with respect to several demographics and risk factors. In particular, the meth and cocaine use class had the highest proportion of females, engagement in sex work, and number of casual sexual partners, but the lowest frequency of heroin injecting.
Conclusions: Qualitative subtypes of heroin IDUs were identified based on meth and cocaine use patterns. Bivariate analyses indicated that a subtype of meth and cocaine users exhibited higher risk sexual practices and lower heroin injecting frequency supplemented by their polydrug use. These findings have identified a subtype of heroin injectors who require more tailored interventions to reduce the health and social harms of injecting drug use in Tijuana.
Financial Support: T32 DA023356

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LOSS AVERSION IS ASSOCIATED WITH COCAINE USE AND RISKY BEHAVIOR IN HIV-INFECTED ADULTS.

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Aims: Cocaine users are more likely than non drug users to engage in risk behaviors associated with HIV infection and transmission. Loss aversion, a behavioral economics concept, describes the tendency for individuals to shy away from potential losses more than they seek potential gains. This study tests the hypothesis proposed by Tom et al (2007, Science) that diminished loss aversion is associated with substance use and other "risky" behaviors.
Methods: Participants were HIV-infected men and women. Loss aversion was assessed using a computerized task in which participants indicated their willingness to gamble on 64 trials that have a 50% chance of winning $12-40 or losing $6-20 and computed as λ= -βloss/βgain, where higher scores indicate greater loss aversion. A "healthy" adult is expected to have a score of ~2. Participants also completed self-report measures of recent substance use, sexual risk behavior, HIV medication adherence, and problem gambling.
Results: To date, the sample includes 28 cocaine users and 34 non-drug users. While the groups were equally likely to accept gambles (both M= 55%), cocaine users demonstrated greater loss aversion than non-drug users (M= 3.51 vs. 1.94; t= 2.13, p= .037). Participants who endorsed symptoms of problem gambling had higher loss aversion scores than those who did not (M= 3.76 vs. 2.06; t= 2.14, p= .035). Furthermore, among cocaine users, loss aversion was positively correlated with sexual risk behavior (r= .39, p= .035) and increased likelihood of missing HIV medications (M= 5.54 vs. 2.52; t= 2.00, p= .056). Loss aversion was a stronger predictor of these risk behaviors than other measures of risk taking propensity, including the Balloon Analogue Risk Task, Iowa Gambling Task, and Monetary Choice Task.
Conclusions: Contrary to hypothesis, cocaine users were more loss averse than non-drug users, possibly because they are less sensitive to both losses and gains. Moreover, our data suggest that loss aversion is a relevant construct for understanding HIV transmission risk behavior among cocaine users.
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IMPLEMENTING EVIDENCE-BASED PSYCHOSOCIAL THERAPIES FOR SUBSTANCE USE: ASPECTS OF MEASURING ADHERENCE AND COMPETENCE.

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Aims: Ensuring treatment quality is a major concern in the implementation of EBTs for substance use disorders. There is wide variation in methods for assessing therapy quality. Most studies use research funding to systematically audit taped sessions, and then utilize structured rating scales. Such research-quality approaches may be cost and workflow prohibitive for community agencies. The present study examines three aspects to assessing clinician adherence and competence. We test the following hypotheses: 1) Clinicians deliver and sustain quality differentially by therapy type and predicated by clinician background factors; 2) Adherence/competence ratings are associated with outcomes; and 3) Statistical modeling techniques can articulate efficient quality monitoring strategies.
Methods: 16 clinicians from six community addiction treatment programs delivered either integrated cognitive behavioral therapy (ICBT) or individual addiction counseling (IAC) to eligible participants meeting criteria for substance use and posttraumatic stress disorders (PTSD). Participants were randomized to either ICBT or IAC, and clinicians were crossed (i.e. delivered both study therapies). Audio-tapes of 25% of all sessions were rated using adherence/competence scales. Therapeutic alliance, number of sessions attended, and patient outcomes were assessed at baseline, 3- and 6-months.
Results: Differences in adherence/competence by therapy type were minimal. Clinician background characteristics and motivation predicted initial quality. The relationship between therapy quality and participant process and outcome measures, and statistical models for measuring quality are presented.
Conclusions: Effective implementation of EBTs may be improved if we consider these background and motivational factors in clinician selection, and by using the efficient approaches to quality monitoring suggested by this study.
Financial Support: Funded by NIDA (RO1DA027650) (PI: McGovern).

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A LONGITUDINAL STUDY OF ADOLESCENT GIRLS' MEDICAL MISUSE AND NON-MEDICAL USE OF CNS DEPRESSANTS.

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Aims: Aims: To determine whether adolescent girls' medical use of opioid analgesics, anxiolytics, or sleeping medications (CNS depressants) at Time 1 leads to an increase in medical misuse and nonmedical use of these medications at Time 2 and Time 3. To further determine whether adolescent girls with a recent prescription for a CNS depressant would have a greater likelihood of self-treating with the medication when compared to adolescents without a recent prescription.
Methods: Methods: A three-year, longitudinal sample of 2014 adolescents attending secondary schools in southeastern Michigan. The ethnically diverse sample had a mean age of 14.3 years; 50.5% was female. The sample self-selected into three groups relative to whether they had a past or current prescription to a CNS depressant: Group A (no prescription), Group B (lifetime, but no current prescription) and Group C (recent prescription).
Results: Results: As hypothesized, Group C had significantly greater odds ($p<.01$) of medical misuse and nonmedical use when compared to Group A; however, this was not true for Group B. Compared to girls in Group A, girls in Group C were nearly 2 times more likely to engage in nonmedical use at Time 3 (AOR 1.89; 95% CI, 1.12-3.21; $P<0.05$). The odds of girls in Group C engaging in nonmedical use for self-treating were two times higher at Time 2 (AOR 2.0; 95% CI, 1.28-3.15; $P<0.01$) and Time 3 (AOR 2.91; 95% CI, 1.32-6.40; $P<0.01$) and their odds of engaging in medical misuse for self-treating were three times higher at Time 3 (AOR 3.05; 95% CI, 1.21-7.72; $P<0.05$).
Conclusions: Conclusions: Recent exposure to CNS depressant medications appears to be a risk factor for adolescents' medical misuse and nonmedical use that is more pronounced among girls, especially girls misusing to self-treat. Further research is needed to better understand this phenomenon.
Financial Support: Financial Support: Research grants R01DA024678, R01DA031160 and T32 DA007267 from the National Institute on Drug Abuse, National Institutes of Health.

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IMPULSIVE CHOICE BEHAVIOR AND SENSORIMOTOR FUNCTION IN ADULT RATS EXPOSED TO CHRONIC INTERMITTENT ETHANOL DURING ADOLESCENCE AND ADULTHOOD.

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Aims: Binge drinking during adolescence and adulthood may have differential long-term effects on the brain.
Methods: This study compared the effects of chronic intermittent ethanol (CIE) exposure on acoustic startle response and light-potentiated startle (LPS) during withdrawal from CIE exposure in adult and adolescent Wistar rats. The impulsive choice behavior was evaluated under baseline conditions and in response to ethanol challenges in CIE-exposed rats during adulthood using the delayed discounting task (DDT). Adolescent and adult rats received 5 g/kg of 25% (w/v) ethanol three times a day, 2 days on/ 2 days off.
Results: During CIE exposure, body weights of adolescent and adult CIE-exposed rats were lower compared to water-exposed rats. CIE exposure produced high levels of intoxication, but the adult group was more sensitive to the sedative effects of ethanol and received lower ethanol doses throughout CIE exposure. Blood ethanol concentrations during CIE exposure were similar in adolescent and adult rats. Independent of age, the startle amplitude was decreased on either day 1 or day 10 of ethanol withdrawal from CIE exposure; while there was no effect of ethanol withdrawal on LPS in all rats. During no stimulus trials, the activity counts in the startle chamber were increased in CIE- exposed adult, but not adolescent rats on day 1, but not day 10, of withdrawal indicating early withdrawal-associated tremor. During the DDT acquisition there was a transient decrease in impulsive choice behavior in rats exposed to CIE during adolescence, but not in CIE-exposed adult rats, but this effect dissipated with extensive training. Ethanol challenge increased impulsive choice in the CIE-exposed adolescent group and had no effect in the CIE-exposed adult group.
Conclusions: CIE exposure during adolescence may increase vulnerability to develop alcohol dependence during adulthood due to diminished signs of ethanol intoxication and withdrawal and increases in impulsivity during re-exposure to ethanol.
Financial Support: NIH grant U01-AA019970-NADIA (AM), UC MEXUS-CONACYT fellowship (JMT)

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ANATABINE SIGNIFICANTLY DECREASES NICOTINE SELF-ADMINISTRATION.

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Aims: Nicotine addiction is associated with a number of lethal disorders (cancer, cardiovascular and pulmonary disease) that result in an estimated >450,000 deaths annually in the United States alone. Relapse rates are high, and more effective medications to aid smoking cessation attempts are urgently needed. We describe a novel approach to medication-based treatment of nicotine addiction in a nonhuman primate model of nicotine self-administration. Anatabine is one of the most abundant of the minor tobacco alkaloids, but relatively little is known about its interactions with the abuse-related effects of nicotine.
Methods: The acute effects of anatabine (0.18-3.2 mg/kg, IM) or saline on nicotine- and food-maintained responding were examined in four rhesus monkeys. Nicotine (0.01 mg/kg/inj, base) and banana-flavored food pellets (1g) were available under a second-order schedule (FR 2, VR 16:S). Anatabine or saline injections were administered 15 min before the food self-administration session began. Saline control treatment was in effect after administration of each anatabine dose.
Results: Anatabine dose-dependently reduced nicotine self-administration ($P<0.05$) with no significant effects on food-maintained responding. Systematic behavioral assessments following each treatment session revealed no evidence of sedation or agitation that could disrupt operant responding. Each monkey returned to baseline levels of nicotine self-administration before administration of the next dose of anatabine, so catheter malfunction could not account for the significant decreases in nicotine self-administration observed.
Conclusions: These data suggest that anatabine could be an effective medication for treatment of nicotine addiction.
Financial Support: Supported by DA026892 from the National Institute on Drug Abuse, NIH.

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THE DUAL DIAGNOSIS CAPABILITY AND MEDICALLY INTEGRATED CARE (DDMICE) INSTRUMENT.

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Aims: To provide an objective, standardized measure of medical care capacity for substance abuse treatment (SAT) and behavioral health (BH) settings; the Dual Capability and Medically Integrated Care (DDMICe) is designed to (a) enable objective assessments of variation in the delivery of primary medical care, and (b) provide a basis for improving the integration of care. Development of the DDMICe: The DDMICe was developed on the basis of a literature review of state regulations for the delivery of medical services in SAT and BH settings. Additionally, a panel of eight stakeholders consisting of physicians, SAT and BH program directors, consumer advocates, and ATTC personnel were surveyed using a modified Delphi method. Low scoring items were eliminated. The DDMICe was then pre-tested on an SAT and a BH program. Description of the DDMICe: The format and standardized administration and scoring of the DDMICe including the use trained observers were the same as those for sister instruments currently in use (e.g., Dual Diagnosis Capability in Addiction Treatment [DDCAT] and related instruments). Items also fell into the same 7 domains as the DDCAT providing a consistency of measurement. Three additional domains for infectious disease were developed based on NIDA's Screen, Test, Treat, and Retain (STTR) model. The total instrument consists of 63 observational items and 10 domains: Program Structure, Program Milieu, Clinical Process (Assessment), Clinical Process (Treatment), Continuity of Care, Staffing, Training, Infectious Disease Prevention, Treatment and Retention of HIV/AIDS, and Treatment and Retention of HepC.
Conclusions: Future steps include establishing the psychometric properties of the DDMICe and developing an implementation model for technical assistance to help SAT and BH programs integrate primary medical care and wellness activities.
Financial Support: This research supported by New York State Health Foundation awards 2008-2496857, 2009-3426912, & 11-20788

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DEVELOPMENT AND TESTING OF A WEB-ENABLED COGNITIVE/NEUROPSYCHOLOGICAL EVALUATION SYSTEM FOR SUBSTANCE ABUSERS.

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Aims: Although methamphetamine (MA) addicts have cognitive impairments the relationships between cognitive functions and relapse have been hard to define in part due to the absence of an easily deployed and accurate testing platform that can be used in field (out of lab) settings. We developed a web-based nuerocognitive testing platform deployed on an iPhone to assess cognitive performance in the field; in this study we compared field and lab performance on three cognitive tests – the Stroop, N-Back and the Stop Signal task - in MA addicts and controls.
Methods: 20 healthy controls and 12 MA addicts underwent in-lab cognitive testing on a validated computerized platform and on an iPhone with an App designed to administer the same tests. Subjects were then sent home with the iPhone and performed the same cognitive tests twice daily over a 2-week period. Subjects also rated ease of use and field performance of the cognitive tests using the smartphone.
Results: N-Back and Stop-Signal results using the portable implementation were comparable to results achieved with the validated test implementation in the laboratory. Patients enjoyed using an implementation of the tests on a portable device. We used a novel implementation of the Stroop task that relied on speech recognition to detect subject response. Unfortunately, we found that while it was possible to obtain reasonable response recognition accuracy, even in the field, the response time measured by the speech recognition engine was not precise enough to yield quantifiable results. There were no differences between MA addicts and controls either in the laboratory or in the field.
Conclusions: Smartphone-based implementation of neurocognitive tasks performed in the field leads to results which are equivalent to those obtained in a laboratory setting, as long as the tasks are appropriate for the environment and tailored appropriately.
Financial Support: Supported by NIDA SBIR HHSN271201000028C

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ROLE OF PROENKEPHALIN AND BETA-ENDORPHIN IN SUCROSE PALATABILITY.

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Aims: Opioid neurotransmission has been implicated in mediating the rewarding effects of palatable foods. Characterization of consummatory behaviors can provide information about reward palatability, as well as changes in palatability due to manipulations in reward value. The goal of this study was to determine the role of endogenous proenkephalin (PENK) and endogenous beta-endorphin (bEND) in mediating palatability.
Methods: To this end, licking microstructure (e.g. total licks, number of lick bouts, average bout lengths) during consumption of sucrose solutions was studied in PENK knockout or bEND-deficient mice using a lickometer. The effects of varying sucrose concentration and food deprivation state were observed.
Results: Compared to wildtype mice, PENK knockout showed decreases in liking bout numbers while bEND-deficient mice showed decreases in mean bout lengths. Furthermore, PENK knockout mice showed decreased changes in weight when introduced to, and removed from, a high fat diet.
Conclusions: These results indicate that PENK and bEND are both involved in appropriate processing of food palatability and associated changes in weight. An understanding of the mechanisms underlying food palatability will be necessary for the development of appropriate treatment strategies targeting pathologies characterized by under- or over-eating.
Financial Support: Supported by Grant #: DA09359; DA05010; DA024635

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SELF-ADMINISTRATION OF NEUROACTIVE STEROIDS BY RHESUS MONKEYS RESPONDING UNDER A PROGRESSIVE-RATIO SCHEDULE OF I.V. MIDAZOLAM INJECTION.

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Aims: Neuroactive steroids (NSs) are natural or synthetic steroids that can rapidly alter the excitability of neurons via $GABA_A$ receptors. We previously have shown that the endogenous (progesterone-derived) NS pregnanolone, but not a synthetic NS (Co 8-7071), was self-administered by rhesus monkeys. Co 8-7071 had discriminative stimulus effects similar to benzodiazepines (BZs). Therefore, its lack of reinforcing effects might be due to DM/PK variables (e.g., duration of action, efficacy differences in parent compound vs.metabolites). In this study, we investigated the reinforcing effects of the synthetic NS ganaxalone (long duration of action) and alphaxalone (short duration of action).
Methods: A progressive-ratio (PR) schedule of i.v. midazolam self-administration was used for determining the reinforcing effects of these NSs, in comparison with BZ-type drugs (alprazolam and zolpidem). Four adult rhesus monkeys were trained to press a lever that resulted in an i.v. midazolam injection (0.056 mg/kg/injection) via a chronic venous catheter. Reinforcing effects of a drug were determined by comparing the average number of injections/session and the average break point (highest response requirement completed in a session) to results from saline tests.
Results: Both NSs were self-administered above levels maintained by saline availability. The maximal level of self-administration, measured by breakpoint, did not differ across the test drugs.
Conclusions: These results demonstrated that two synthetic NSs were self-administered to a degree similar to the BZ-like drugs alprazolam and zolpidem. Because ganaxolone was self-administered and has a relatively long duration of action, the previous demonstration of a lack of reinforcing effects of Co 8-7071 likely was due to pro-drug properties rather than duration of action.
Financial Support: DA011792, DA033795 and OD011103.

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INVESTIGATING GROUP CONTINGENCIES TO PROMOTE BRIEF ABSTINENCE FROM CIGARETTE SMOKING.

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Aims: In contingency management (CM) interventions, monetary incentives are contingent on objective evidence of drug abstinence. Typically, these incentives (e.g., "vouchers") are contingent on individual performance. In the current study, we programmed vouchers contingent on group performance and evaluated an Internet-based group CM intervention to promote smoking cessation.
Methods: Thirty-two participants were divided into teams (n = 3 per team) and submitted breath carbon monoxide measures twice daily via the Internet during three, 5-day within-subject treatment conditions. During the interdependent contingency condition, participants earned vouchers each time they and their teammates submitted negative samples. During the independent contingency condition, participants earned vouchers each time they submitted negative samples, regardless of their teammates' performance. During the no vouchers condition, no monetary incentives were contingent on abstinence. Throughout all three within-subject treatment conditions, half of the participants (n = 16) could communicate with their teammates through an online discussion forum.
Results: Significantly more negative samples were submitted when vouchers were contingent on individual performance (56%) or team performance (53%) relative to when no vouchers were available (35%; $F = 6.9$, $p = 0.002$). Despite similar treatment outcomes between independent and interdependent contingency conditions, costs were much lower during the interdependent contingency condition. Forum access did not improve primary treatment outcomes. However, it did improve treatment acceptability.
Conclusions: This study is the first to demonstrate that interdependent contingencies of reinforcement can be used to promote abstinence from abused substances. Interdependent contingencies may represent a more affordable alternative to independent contingencies in CM interventions.
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INTIMATE PARTNER VIOLENCE AND IRANIAN WOMEN WITH SUBSTANCE USE DISORDERS.

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Aims: Intimate partner violence (IPV) and risky sexual behaviors are serious and overlapping public health problems that disproportionately affect drug-involved women. Despite the fact that drug-using women experience extensive IPV, no studies to date have investigated the association of IPV and risky sexual behaviors among drug-using women in Iran.
Methods: Drug-using women (N=120) were recruited from a rehabilitation center in Tehran from March to October, 2009. The Revised Conflict Tactics Scale (CTS2), a standardized questionnaire, was used to collect data regarding violence.
Results: CTS score for violence in all dimensions was 1.69, with subscale scores: arguments 4.29, psychological violence 2.55, sexual violence 0.37, physical abuse 1.17, and injury 2.18. We found higher injury scores but lower sexual abuse scores among women with sexually-transmitted infection (p-values 0.03 and <0.0001, respectively). In addition, we found that psychological abuse was positively associated with sexually-transmitted infection (p-value 0.03) and increased condom use (p=0.01), possibly mediated through an increased likelihood of having multiple partners.
Conclusions: The findings revealed that drug-involved women in Iran experience high rates of IPV, and that IPV is associated with increased risky sexual behavior. Preventive interventions for violence that are integrated within drug treatment programs, as well as harm reduction programs are highly recommended.
Financial Support: This study (code# 810) was funded by the Tehran University of Medical Sciences.

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THE DIFFERENTIAL EXPRESSION OF MDPV-INDUCED CONDITIONED TASTE AVERSIONS, THERMOREGULATION AND MONOAMINE LEVELS IN ADOLESCENT AND ADULT RATS: A BEHAVIORAL AND NEUROCHEMICAL ASSESSMENT OF "BATH SALTS"

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Aims: The present study used the conditioned taste aversion procedure to determine if MDPV (a primary constituent in "bath salts") induces aversions in rats and if those aversions are age dependent. Core body temperatures and monoamine levels were quantified to determine if MDPV produces hyperthermia/hypothermia or long-lasting changes in neurotransmitter levels and if these indices are related to aversions.
Methods: Adolescent (PND 21) and adult (PND 78) rats were compared in their ability to acquire taste aversions and in thermoregulation induced by MDPV (0, 1.0, 1.8 or 3.2 mg/kg IP). Monoamine and associated metabolite levels in several brain regions were measured using HPLC following acute MDPV exposure.
Results: Although MDPV induced aversions in both age groups, these effects were less robust in the adolescent subjects (during acquisition and on a subsequent two-bottle assessment). Core body temperature measurements also differed with adults exhibiting hyperthermia and adolescents exhibiting hypothermia following acute exposure to MDPV. Overall neurotransmitter levels differed primarily as a function of age, although MDPV induced minor changes in dopamine levels in adult subjects.
Conclusions: Like other drugs of abuse, MDPV appears to have both rewarding and aversive effects that differ with age. These effects did not appear related to specific changes in core temperature or monoamine levels. Given that drug taking behavior is a function of the relative balance between the drug's rewarding and aversive effects, the fact that the aversive effects are weaker in adolescents suggests that adolescents may be more vulnerable to MDPV use and abuse.
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TRAUMA-INFORMED TREATMENT DECREASES PTSD AMONG WOMEN OFFENDERS.

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Aims: To examine the trauma histories and prevalence of PTSD among women offenders in gender-responsive and trauma-informed substance abuse treatment and assess their change in symptomatology over time. Women in gender-responsive treatment (GRT; n = 134) were compared to women in non-GRT (n = 143).
Methods: This study combined data from 2 previous studies of women offenders using the same measures. The data for these analyses were collected between 2007 and 2011. Both studies' enhanced treatment programs followed the principles of a gender-responsive treatment (GRT) model, incorporating trauma-informed curricula and other services oriented towards the needs of women.All procedures were reviewed and approved by the UCLA General Campus IRB. The PDS was used to determine a current diagnosis of PTSD (Foa, 1997).
Results: The pooled sample of women were predominantly White (58%) or Hispanic (22%) and many had never been married (47%); their mean age was 36 years (SD = 8.9), and, on average, they had 12 years (SD = 1.8) of education. Methamphetamine was their primary drug (71%). Fifty-five percent of the women reported histories of sexual abuse and 37% physical abuse. Thirty-one percent had a PTSD diagnosis. Using GEE, significant group by time interactions were detected in PTSD (OR = .17) and some related symptomatology (re-experiencing: OR = .42, and avoidance: OR = .24).
Conclusions: The repeated measures analysis showed significant interaction effects between group and time-point for three of the five models (change in PTSD, re-experiencing, and avoidance). The finding that the GRT group of women had a reduction in their diagnosis of PTSD and some related symptomatology is important, as there is currently great debate over addressing trauma histories during substance abuse treatment.
Financial Support: This study was funded by the National Institute on Drug Abuse (NIDA Grant No. R01 DA22149-01), the California Department of Corrections and Rehabilitation (Contract No. C06.441), and the California Endowment (Grant No. 20081206).

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DEVELOPMENT AND INITIAL VALIDATION OF A MARIJUANA CESSATION EXPECTANCY SCALE.

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Aims: Longitudinal research indicates that a portion of substance users make efforts and actually reduce or stop marijuana use (e.g., Copersino et al., 2006; Ellingstad et al., 2006). Substance-related cognitions, particularly expectancies leading to such efforts, may significantly inform and improve substance abuse treatment programs. The present research examines anticipated consequences of ceasing or reducing marijuana use with initial development and psychometric validation of a measure of marijuana cessation expectancies (MCE).
Methods: Based on the content validity analysis of the free response cessation expectancy data, a scale of forty-six items was administered to 254 non-treatment seeking regular marijuana users (mean age = 21; 36% female; mean possible marijuana use days = 67.6%, SD= 23.9).
Results: Exploratory factor analyses identified expectations related to performance motivation, negative emotions, eating, problems with authority, and physical activity, accounting for 61% of variance. All factors and full scale had good internal consistency (alphas=.62 to .86). Patterns of expectancies reflected beliefs that cutting down or stopping marijuana use would enhance motivation and performance-related skills but would also increase negative affective states. Performance motivation scores were significantly associated with number of marijuana-related problems ($r = .59$, $p < .001$) and history of marijuana quit attempts ($r = .20$, $p = .001$), with 51% of the sample reporting having tried to reduce marijuana use and 28% reporting having made quit attempts. Negative emotion scores were significantly associated with frequency of marijuana use ($r = -.26$, $p < .001$) and number of marijuana quit attempts ($r = -.14$, $p < .05$). Additional support for convergent validity of the MCE measure was established with significant associations with marijuana outcome expectancies and use motives.
Conclusions: These data provide initial support for the MCE measure and suggest it may be useful for clarifying the role of cessation expectancies in marijuana change efforts.
Financial Support: R01 DA021403 (Metrik) and R03DA027484 (Metrik, Knopik)

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FAVORABLE OUTCOMES IN NEWBORNS PRENATALLY EXPOSED TO BUPRENORPHINE COMPARED TO METHADONE AND SLOW-RELEASE ORAL MORPHINE.

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Aims: This study investigated outcome parameters in newborns of opioid-dependent women (DSM IV 304.00) undergoing opioid maintenance therapy during pregnancy in the frame of standardized multi-disciplinary treatment at the Medical University of Vienna, Austria.
Methods: An observational design was applied to evaluate the outcome of 390 singleton pregnancies of treatment completers (81.6% of 478) maintained on methadone (47.2%, mean dose at delivery=64mg/SD=36mg), buprenorphine (19.7%, 10mg/6mg) or slow-release oral morphine (SROM; 33.1%, 455mg/207mg). Newborns were assessed for neonatal abstinence syndrome (NAS) by the application of a modified Finnegan Scale. NAS was treated using morphine hydrochloride (62.4%), phenobarbital (5.5%) or a combination of medications (32.1%). One-way analysis of variance (ANOVA) was used to test for differences in continuous variables among the three opioid medication groups, Chi-square tests or Fisher's Exact test for categorical data.
Results: Newborns exposed to buprenorphine showed significantly higher birth weight (mean 3007g/SD=569g) compared to the methadone-exposed group (2774g/504g, p=0.004), but not compared to the SROM-group (2845g/562g, p=0.092); they had the lowest rate of premature births (9.1% vs. 27.2% in the methadone group and 27.1% in the SROM group, p=0.004), and the smallest proportion requiring pharmacological NAS treatment (57.3% compared to 73.4% in the methadone-exposed group and 86.6% in the SROM-exposed group, p<0.001). Buprenorphine-exposed infants had the lowest NAS scores of all 3 groups (p<0.001), required the least amount of pharmacological treatment (p<0.001), and had the shortest treatment duration (p<0.001) and hospital stay (p<0.001).
Conclusions: Patients undergoing standard treatment show results that are in line with findings of recent clinical trials, confirming the favorable outcome of children prenatally exposed to buprenorphine compared to methadone or SROM.
Financial Support: This research was supported by the following grants: R01DA018417 (NIDA)
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CHALLENGES TO RECRUITMENT OF COCAINE-USING WOMEN FOR A MEDICATION DEVELOPMENT TRIAL.

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Aims: Epidemiological data indicates that cocaine using women are at high risk for HIV infection. There has been a significant amount of effort devoted to the development medications to aid in the treatment of cocaine abuse and dependence. Here we report on the enrollment challenges encountered in the recruitment of women testing the efficacy of modafinil in the treatment of cocaine abusing women.
Methods: We used screening and enrollment data from a clinical trial designed to measure the impact of modafinil on cocaine use and related risk behaviors. Recruitment was community based and utilized a mobile clinical trials unit (MCTU) that provided convenient, confidential space for conducting interviews and a fully equipped exam room for all medical procedures. Three recruitment locations were established that offered easy access to target population of cocaine (primarily crack) abusers.
Results: Between July 2008 and March 2009, a total of 316 cocaine abusing (primarily crack smokers) women were screened in the community to assess eligibility and willingness for enrollment in the trial. Of these, only 40 women were found to be eligible after satisfying the inclusion and exclusion criteria. The reasons for ineligibility were as follows: 146 (45%) were not sexually active in prior 30 days, 93 (29%) had co-occurring alcohol dependence, 24 (7.4%) were dependent on drugs other than cocaine and 81 (25%) has serious mental illness.
Conclusions: While there is an urgent need for developing new and effective treatments for cocaine using women at high risk for HIV, the co-occurring, behavioral, substance use, and psychiatric characteristics of this group limit their participation in medication trials. Our results highlight this paradox. Future clinical trials need to be sensitive to the inclusion of these women so as to facilitate development and testing of appropriate treatment mechanisms.
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CHARACTERIZING PRESCRIPTION OPIOID ABUSERS WITH AND WITHOUT LIFETIME HEROIN USE.

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Aims: While research suggests primary prescription opioid (PO) abusers may exhibit less severe demographic and drug use characteristics than heroin abusers, little is known about whether lifetime heroin use is associated with greater severity among treatment-seeking PO abusers. This study compared demographic, psychosocial and drug use characteristics of PO abusers with and without a history of regular heroin use.
Methods: Participants were 89 PO-dependent adults evaluated for a randomized trial evaluating buprenorphine taper and subsequent naltrexone maintenance. Participants were dichotomized based on self-reported lifetime heroin use ≥5 (H^+; n=41) or <5 times (H^-; n=48).
Results: H^+ participants were older (30 vs. 26 yrs; p=.003) and more likely to be male (81 vs. 54%; p=.01) compared to H^- participants. They scored lower on the positive symptom distress index (1.52 vs. 1.75; p=.03) and depression subscale (.82 vs. 1.19; p=.04) of the Brief Symptoms Inventory. While PO use was generally similar between the groups, as expected more H^+ than H^- participants reported lifetime (100 vs. 23%; p<.001) and past-month (10 vs. 0%; p=.03) heroin use, as well as a longer duration of heroin use (1.6 vs. 0.01 yrs; p=.05). H^+ participants also had a longer duration of regular illicit opioid use (6 vs. 4 yrs; p=.01) and a greater percent reported lifetime IV drug use (76 vs. 15%; p<.001) than H^-. Several differences in non-opioid drug use were also seen. More H^+ participants reported lifetime cigarette (98 vs. 85%; p=.05), amphetamine (46 vs. 25%; p=.04) and hallucinogen (59 vs. 31%; p=.01) use, as well as past 30-day cocaine use (29 vs. 13%; p=.05). H^+ participants reported more alcohol-related problems, evidenced by higher Michigan Alcohol Screening Test scores (12 vs. 6; p=.002).
Conclusions: These data suggest that, at least in a population of treatment-seeking PO abusers, a lifetime history of heroin use may be associated with elevated drug use severity. Further research is warranted to extend these findings to broader populations of PO abusers, as well as evaluate implications for treating PO abusers.
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RESIDENTIAL INITIATION OF EXTENDED-RELEASE NALTREXONE AND FOLLOW-UP IN OPIOID-DEPENDENT PATIENTS VS. CASE-MATCHED CONTROLS.

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Aims: A naturalistic study of the effectiveness & costs of XR–NTX for opioid dependence initiated during residential rehabilitation.
Methods: Retrospective examination of electronic records at 3 PA-based detox/rehab sites owned by CRC Health Group. We compared 2 groups that were Medicaid supported and referred for intensive outpatient treatment at a Pennsylvania CRC site: XR-NTX vs. non XR-NTX (n=75 each): case-mix adjusted, using demographic, clinical and service parameters. We reviewed discharge summaries and OPD records for adherence to injections and outpatient care, drug use and estimated healthcare costs.
Results: 7,687 opioid dependent patients admitted in 2011; 430, XR-NTX recommended but not received; another 168 patients did receive XR-NTX. Medicaid covered 84.5% (n= 142) of XR-NTX patients, who were more likely to complete inpatient (93.5% vs. 63.0%; p<.001). Only 4.8% of the XR – NTX treated group were discharged against medical advice vs. 30.2% (p<.001). Data were further analyzed on OPD outcomes of randomly selected 75 XR-NTX pts. & case-mix adjusted controls .
Conclusions: This is the first effectiveness & cost analysis study of XR-NTX for opioid dependence in a Medicaid cohort. Data indicate improved Pt completion of inpatient care with XR-NTX. Further data analysis using a case-matched control group examined treatment adherence in OPD, drug use & psychosocial functioning, & the estimated relative costs of the specific treatments received by each cohort. The findings have potential policy ramifications.
Financial Support: Supported by a research services agreement from Alkermes Inc., to Penn State University. Dr. Herschman is an employee of CRC Health Group, Inc. Dr. Gastfriend is a full-time employee of Alkermes. XR-NTX (VIVITROL®) was developed with grants from NIDA (R43DA013531) & NIAAA (N43AA001002).

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EXAMINING POLYGENIC RISK OF CIGARETTE USE IN THE DETROIT NEIGHBORHOOD HEALTH STUDY.

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Aims: Cigarette smoking is influenced both by genetic and environmental factors (Broms et al., 2006). Until this year, all large-scale gene identification studies on smoking were conducted in populations of European descent. Recently, a meta-analysis of smoking in 32,389 African-Americans was conducted (David et al., 2012). This study produced one genetic variant of genome wide significance and eight additional variants that were approaching significance. The stringent significance threshold, put in place to protect against high rates of false positives, demands that in order to detect a statistically significant signal, large, ethnically homogeneous samples are required. This motivates the further investigation of the top variants reported in this meta-analysis in the Detroit Neighborhood Health Study (DNHS), 1,306 randomly selected majority African American residents of Detroit, with DNA collected on 778 individuals.
Methods: In the DNHS, we have constructed a genetic risk score (GRS) in which we have combined these top genetic variants, in an effort to more accurately model the genetic architecture of smoking behaviors and potentially account for a greater portion of the variance in these traits.
Results: Among individuals who had been exposed to nicotine, had data available on cigarette use and DNA collected, the GRS significantly (beta=.14, p-value= .04) predicted cigarettes per day and accounted for ~3% of the overall variance in the trait. In addition, significant interactions were observed between this GRS and several aspects of the individual's social context, including social cohesion and experiencing traumatic events.
Conclusions: Because of the sample size, this study is limited in the potential strength of the association signal, however this study provides support for the utility of the GRS as an alternative approach to replication of common polygenic variation, and gene-environment interactions, in smoking behaviors.
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MODELING INTER-RELATIONSHIPS AMONG LONGITUDINAL NON-NORMAL OUTCOMES: TRAJECTORIES OF DAILY USE OF DIFFERENT DRUGS DURING TREATMENT.

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Aims: Ample research shows high rates of polysubstance use in adolescents. Daily use outcomes widely collected via Timeline Followback (TLFB) are non-normal, limiting analytic methods for evaluating inter-relationships. We: (1) develop methods to simultaneously analyze multiple non-normal longitudinal outcomes such as trajectories of daily drug use and (2) use those methods to estimate associations among daily marijuana, cigarette, and alcohol use in data from a Clinical Trials Network pharmacotherapy trial for ADHD and drug use in adolescents (CTN28).
Methods: We extend a multivariate longitudinal model for binary (used alcohol yes/no) and count (joints and cigarettes per day) data to estimate covariances among random effects for calculating subject-specific correlations and partial correlations in baseline use and rates of change of use. We estimate correlations at specific times to determine whether change in use of one drug is associated with earlier/subsequent change in use of another and stronger earlier/later in treatment. Analyses use CTN28 trial-completers who were regular users of each drug at baseline.
Results: Adolescents' daily marijuana joints and cigarettes smoked (n=66) are minimally associated at baseline (r=0.20, NS) and in their change in use during treatment, adjusting for baseline (r=0.27, p=.04). Daily joints smoked and alcohol use (n=65) are associated at baseline (r=0.30, p=.03) and in their change in use during treatment, adjusting for baseline (r=0.31; p=.04). Correlations with marijuana use are strongest for same day or earlier cigarette use at baseline (r's >= 0.20) and for same day or later alcohol use near treatment end (r's >.41).
Conclusions: Adolescent patients' daily marijuana use is more associated with alcohol use than cigarette use, both at baseline and in how use changes during treatment. Marijuana's association with cigarettes is strongest at baseline and with alcohol is strongest later in treatment. Statistical methodology developed here has important utility beyond this specific application.
Financial Support: DA034604, DA022284, DA013732

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ALCOHOL ENVIRONMENT, PERCEIVED SAFETY, AND EXPOSURE TO ALCOHOL, TOBACCO, AND OTHER DRUGS IN EARLY ADOLESCENCE.

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Aims: This study examined the association between the count of alcohol outlets around children's homes and opportunities to use alcohol, tobacco, and other drugs (ATOD) as well as perceived safety during pre-adolescence. We hypothesized that the greater the density of alcohol outlets, the more likely the youth would be to have opportunities to use ATOD.
Methods: Data were collected in 2007 from 394 Baltimore City children aged 8-13 (86% African American). Participants' residential address and alcohol outlet data were geocoded with quarter mile (i.e., walking distance) buffers placed around each participant's home to determine the number of outlets within walking distance.
Results: The unadjusted logistic regression models revealed that each unit increase in the number of alcohol outlets was associated with a 14% increase in the likelihood of children seeing people selling drugs (OR=1.14, p=.04) and a 15% increase in the likelihood of seeing people smoking marijuana (OR=1.15, p<.01). The number of alcohol outlets was also associated with 21% increase in the likelihood of children feeling unsafe in their neighborhood (OR=1.21, p<.01). After adjusting for individual level covariates (i.e. age, gender, socioeconomic status), the relationship between the alcohol outlet count and seeing people smoking marijuana as well as perceived safety remained significant (OR=1.11, p<.01 & OR=1.20, p<.01, respectively). However, after adjusting for neighborhood physical disorder, a proxy for neighborhood disadvantage, the relationship between alcohol outlets and seeing people smoking marijuana as well as perceived neighborhood safety was fully attenuated.
Conclusions: These results suggest that alcohol outlets are one aspect of the larger environmental context that is related to ATOD exposure in children. Future studies should examine the complex relationship between neighborhood physical disorder and the presence of alcohol outlets.
Financial Support: NIAAA-R01AA015196 & NIDA-R01DA018318

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EFFECTS OF PLASMA ALLOPREGNANOLONE LEVELS ON DRUG CRAVING IN COCAINE-DEPENDENT MEN AND WOMEN.

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Aims: Fluctuations in progesterone levels during the menstrual cycle have been shown to affect physiological and subjective effects of cocaine. Furthermore, our laboratory has demonstrated that following drug-cue exposure, women with high levels of circulating progesterone display lower diastolic and systolic blood pressure responses and report lower levels of anxiety and drug craving compared to cocaine dependent (CD) women with low levels of progesterone. However, the role of the neuroactive progesterone metabolite allopregnanolone (allo) in the effects of cocaine craving has not been systematically examined.
Methods: Plasma levels of the neuroactive steroid allo were measured using GC/MS in 26 treatment-seeking CD men and women after either daily doses of placebo (9M/4F) or micronized progesterone (7M/6F) (400mg/day) for 7 days administered in a double blind, randomized manner. All subjects were exposed to a 5-min personalized guided imagery to stress, cocaine-cue and neutral imagery in a 3-day laboratory experiment on days 5-7 of progesterone/placebo administration. Subjective craving was assessed before and after imagery and a change-in-craving score was generated.
Results: Progesterone relative to placebo significantly increased allo levels (p<0.001). In addition, CD men experienced a larger increase in allo in response to progesterone treatment compared to CD women (p=0.023). Finally, individuals with high compared to those with low allo levels had a significantly smaller craving response to cocaine cue imagery (p=0.021).
Conclusions: Progesterone significantly increased allo plasma levels in CD individuals, and this effect was further enhanced in men. Increased plasma levels of allo were associated with a decreased craving response to cocaine-cue imagery, irrespective of gender. These findings suggest that progesterone, arguably via its conversion to allo, may be effective in reducing cocaine-cue induced craving.
Financial Support: P50-DA016556

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ACTIVE VACCINATION INHIBITS THE ACQUISITION OF METHAMPHETAMINE SELF-ADMINISTRATION IN RATS.

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Aims: D-methamphetamine (METH) addiction is a serious public health concern for which successful treatment remains elusive. Immunopharmacotherapy has been shown to attenuate locomotor and thermoregulatory effects of METH. The aim of the current study was to investigate whether active vaccination against METH could alter intravenous METH self-administration in rats.
Methods: Male Sprague-Dawley rats (N=24) were vaccinated with either a candidate anti-METH vaccine (MH6) or a control keyhole-limpet hemocyanin conjugate vaccine (KLH). Effects of vaccination on the acquisition of METH self-administration under 0.1 mg/kg/inf and across a range of doses of METH (0, 0.01, 0.05, 0.20 mg/kg/inf) during steady-state responding were investigated.
Results: Active vaccination inhibited the acquisition of METH self-administration under the 0.1 mg/kg/inf dose condition, with 66% of the MH6-vaccinated rats compared to 100% of the controls reaching criteria, and produced transient and dose-dependent effects on self-administration during the maintenance phase.
Conclusions: These data demonstrate that active immunopharmacotherapy for METH inhibits the acquisition of METH self-administration.
Financial Support: Supported by NIH/NIDA grant #DA024705

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BEHAVIORAL ADJUSTMENT IN PRENATALLY COCAINE-EXPOSED ADOLESCENTS.

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Aims: To assess differences in self-reported behavioral adjustment in prenatally cocaine exposed (PCE) and non-cocaine exposed (NCE) adolescents at ages 12 and 15 years.
Methods: Adolescents (N=371; 189 PCE, 182 NCE), primarily African-American and low socioeconomic status, were prospectively enrolled in a longitudinal study at birth (92% retention). The Youth Self-Report (YSR) was used to assess behavioral adjustment. A mixed model repeated measures analysis was used, controlling for covariates including other prenatal drug exposures and lead.
Results: Adolescents with PCE reported greater externalizing problems (adjusted mean ± SE: 49.9 ± 0.78 vs. 47.3 ± 0.76 at 12; 52.6 ± 0.86 vs. 50.2 ± 0.84 at 15) than NCE adolescents ($p < .02$) after control for covariates. PCE adolescents reported increased inattention at 15 year (59.4 ± 0.68 vs. 57.3 ± 0.67; $p < .03$) compared to NCE adolescents. No PCE effect on internalizing problems was found. All externalizing, internalizing, and attention problem scores increased from 12 to 15 years. Girls reported a greater increase in externalizing and internalizing problems from 12 to 15 years than boys. Greater maternal psychological distress was related to higher internalizing problems ($p=.03$). Greater parental monitoring was related to fewer externalizing problems; greater family conflict was related to more externalizing and attention problems; and greater violence exposure was related to more externalizing and internalizing problems. Prenatal marijuana exposure was related to inattention ($p <.02$). Marginal effects of prenatal alcohol on internalizing behavior ($p=.07$) and blood lead on inattention ($p=.051$) were found.
Conclusions: PCE is related to externalizing problems and inattention in adolescence. Interventions focusing on strengthening parental monitoring and decreasing family conflict and violence exposure may be promising in reducing behavioral problems among high risk adolescents with PCE.
Financial Support: National Institute on Drug Abuse Grant R01-07957

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EXECUTIVE FUNCTION IN CHILDREN WITH PRENATAL COCAINE EXPOSURE AT 12 AND 15 YEARS.

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Aims: To examine between and within group differences in executive function (EF) in prenatally
cocaine exposed (PCE) and non-cocaine exposed (NCE) children at 12 and 15 years of age.
Methods: Three hundred seventy (188 PCE, 182 NCE), primarily African American, low socioeconomic
status children participated in a prospective, longitudinal study. The Behavior Rating Inventory of
Executive Function (BRIEF) Parent Form was administered to assess executive function (EF). Broadband T-scores for Behavioral Regulation (BRI), Metacognition (MCI) and Global (GEF) were assessed. A mixed model repeated measures analysis was used, controlling for covariates including other prenatal drug exposures and environmental factors. These analyses were completed separately for males and female based on previous cohort findings.
Results: PCE females showed greater behavioral regulation problems compared to NCE females at 12
years (adjusted mean: 55.45 vs. 50.01, $p=.002$). There was a significant time effect for PCE girls ($p<.04$)and boys ($p<.05$) indicating fewer behavioral regulation problems over time. There were no cocaine effects for boys. For MCI and GEF, there were significant cocaine effects among females at 12 ($p<.001$) and 15 ($p<.04$), and a significant time effect for PCE girls ($p<.03$). A significant negative effect of prenatal alcohol exposure was noted for both males and females on MCI and GEF.
Conclusions: PCE is associated with increased problems of executive function among females only at 12
and 15 years of age. Prenatal alcohol exposure is negatively associated with MCI and GEF. Developing interventions aimed at improving behavioral regulations and metacognitive ability warrant attention for prenatally cocaine exposed females and alcohol exposed individuals of both genders.
Financial Support: This research was supported by the National Institute on Drug Abuse grant (NIDA R0107957)

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ADHD SUBTYPE DIFFERENCES IN SMOKING TO REGULATE AFFECT AND ADHD SYMPTOMS USING ECOLOGICAL MOMENTARY ASSESSMENT.

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Aims: Attention-Deficit/Hyperactivity Disorder (ADHD) is an independent risk factor for cigarette smoking. Although smokers with ADHD differ from non-ADHD smokers in many respects, ADHD is a heterogeneous disorder composed of different subtypes. Given that past research has demonstrated differences between ADHD subtypes, including studies examining nicotine dependence, the aim of the current study was to assess ADHD subtype differences in the immediate consequences of smoking using ecological momentary assessment (EMA). In particular, we aimed to assess subtype differences in smoking to regulate affect and ADHD symptoms.
Methods: Smokers with ADHD ($n = 17$) were subdivided into ADHD Predominately Inattentive ($n = 9$) and ADHD Combined ($n = 8$) subtypes following a diagnostic assessment. Participants carried an electronic diary for at least 7 days and provided entries for each cigarette they smoked.
Results: Both groups did not differ in nicotine dependence severity. 1,232 EMA smoking entries were recorded. Participants responded to questions immediately prior to and after each cigarette. The ADHD Combined subtype reported significantly greater reductions in boredom ($p = .011$), total ADHD symptoms ($p = .019$), inattentive ADHD symptoms ($p = .013$), and hyperactive-impulsive ADHD symptoms ($p = .048$) than the ADHD Inattentive subtype in a series of ANOVA's. In addition, the Combined subtype reported a statistically significant improvement in positive affect after smoking ($p = .038$). Subtypes did not differ in smoking to regulate urge to smoke, negative affect, anxiety, stress, hunger, worry, or general restlessness.
Conclusions: These findings have implications for the role of affect and ADHD symptom regulation in smoking maintenance among ADHD subtypes. Particularly, those with the Combined subtype may smoke to regulate ADHD symptoms, positive affect, and negative affect, whereas those with the Inattentive subtype may smoke to regulate primarily negative affect.
Financial Support: This research was supported by Grant R03DA029694 (John T. Mitchell)

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ADOLESCENT RISK TAKING, DOPAMINE, AND COCAINE: A VICIOUS CYCLE.

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Aims: Adolescents exhibit risky decision-making that may contribute to and/or result from drug use. Causal relationships among adolescent development, risk taking, and drug use are difficult to disentangle in humans; therefore, we used animal models to study these relationships.
Methods: Adolescent male Long-Evans rats (P25) were trained in the Risky Decision-making Task (RDT) in which they chose between two levers: the first delivered a small, "safe" food reward and the second delivered a large, "risky" food reward accompanied by risk of a mild footshock, the probability of which increased over the course of the test session (0, 25, 50, 75, 100%). Upon completion, rats self-administered (SA) 0.5 mg/kg/infusion cocaine for 2h/d for 10 d followed by 1.0 mg/kg/infusion for 6h/d for 14d (or sucrose for a control). Upon completion of SA, rats remained abstinent from cocaine (or sucrose) for 3 weeks before retesting in the RDT.
Results: Individual variability in risk preference predicted cocaine intake during the first 5 days of cocaine SA. Following SA, cocaine SA rats showed greater risk taking compared to sucrose controls well into abstinence. Greater risk taking in adolescence was associated with lower striatal D2 mRNA expression. Intra-striatal microinjections of the D2/D3 agonist quinpirole influenced RDT performance, with ventral, but not dorsal striatal injections resulting in a dose-dependent decrease in risk taking.
Conclusions: Elevated adolescent risk taking predicts greater acquisition of cocaine SA, and cocaine SA in turn causes long-lasting elevations in risk taking. The findings that lower D2R expression in striatum associated with elevated risk taking, and that activation of D2Rs in ventral striatum reduced risk taking suggest that D2Rs may play a causal role in both risk taking behavior and cocaine SA. Together the findings suggest a "vicious cycle" of risk taking and cocaine use which may be regulated by D2Rs and contribute to addictive behaviors.
Financial Support: DA024671 (BS) DA033074 (MRM)

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INDICATORS OF TREATMENT SUCCESS: COMPARING URINE DRUG SCREENING OUTCOMES WITH QUALITY OF LIFE FOR BUPRENORPHINE PATIENTS.

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Aims: To examine the relationship between urine opioid screening test results and changes in self-reported quality of life among opioid-dependent patients entering buprenorphine treatment.
Methods: Participants (N=319) entering buprenorphine treatment were assessed at treatment entry and at 3- and 6-month follow-up with a urine test for opioids and the WHO's Quality of Life-BREF instrument (measuring physical, psychological, social, and environmental domains). A series of general linear mixed models were used to examine the association between urine opioid test results and Quality of Life across the three assessment periods. Control variables included age, gender, time, and treatment retention status at each time point as a time-varying covariate.
Results: Urine opioid testing results were not significantly associated with any of the Quality of Life scales. Significant improvements over time, independent of treatment retention status, were observed for Physical ($p<.05$) and Social ($p<.001$) Quality of Life domains. Being retained in treatment was significantly positively associated with Physical, Psychological, and Environmental Quality of Life domains (all ps <.001). Increasing age and female gender were associated with worse Physical Quality of Life ($p<.05$ and .01, respectively).
Conclusions: Urine opioid testing results have little association with Quality of Life despite the fact that participants report substantial improvements in Quality of Life after entering buprenorphine treatment. Being retained in treatment is associated with higher quality of life in most domains. Urine testing alone may not be a good indicator of global impairment and maps poorly to subjective patient improvement in Quality of Life following treatment. It is important for researchers and clinicians to consider additional metrics beyond urine drug test results for gauging progress in treatment.
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CHOICE TO VIEW COCAINE IMAGES PREDICTS CONCURRENT AND PROSPECTIVE DRUG USE IN COCAINE ADDICTION.

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Aims: Identifying variables that predict drug use in treatment-seeking drug addicted individuals is a crucial research and therapeutic goal. This study tested the hypothesis that choice to view cocaine images is associated with concurrent and prospective drug use in cocaine addiction.
Methods: To establish choice-concurrent drug use associations, 71 cocaine addicted subjects (43 current users and 28 treatment seekers) provided data on (A) choice to view cocaine images and affectively pleasant, unpleasant, and neutral images [collected under explicit contingencies (i.e., choice between two fully visible side-by-side images) and under more probabilistic contingencies (i.e., choice of pictures hidden under flipped-over cards)]; and (B) past-month cocaine and other drug use. To establish choice-prospective drug use associations, 20 of these treatment-seeking subjects were followed over the next six months.
Results: Baseline cocaine-related picture choice as measured by both tasks positively correlated with subjects' concurrent cocaine and other drug use as driven by the actively-using subjects. In a subsequent multiple regression analysis, choice to view cocaine images over pleasant images (under probabilistic contingencies) was the only predictor that remained significantly associated with drug use ($\beta=0.24$, $p<0.05$). Importantly, this same baseline cocaine>pleasant probabilistic choice also predicted the number of days drugs were used (cocaine, alcohol, marijuana) over the next six months ($\beta=0.47$, $p<0.05$). This association survived controlling for other common predictors of relapse (comorbidity, IQ, craving, baseline drug use) (all $p\leq0.05$).
Conclusions: Simulated cocaine choice – especially when probabilistic and when compared with other positive reinforcers – may provide a valid laboratory marker of current and future drug use in cocaine addiction.
Financial Support: Supported by NIDA grants 1R01DA023579 and 1F32DA030017-01.

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EFFECTS OF MINOCYCLINE ON OXYCODONE-INDUCED RESPONSES IN HUMANS.

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Aims: Recent data suggest the importance of glial cell activation in the acute effects of opioids and the development of opioid tolerance. Preclinical studies suggest that acute and chronic opioid administration activates glia and cytokine release, which results in suppression of narcotic analgesic effects. Preclinical studies demonstrate minocycline's abilities to inhibit opioid-induced glial activation, as well as significantly reduce rewarding effects of opioids. Therefore, the purpose of this study was to assess the effects of acute administration of minocycline on the subjective, physiological, and analgesic effects of oxycodone.
Methods: Non-treatment seeking, non-dependent opioid users (N=7) participated in this randomized, within-subject, double-blind outpatient pilot study. Participants completed five separate sessions in which they received 0, 100, or 200 mg minocycline (MINO) simultaneously with either 0 or 40 mg oxycodone (OXY). The subjective, physiological, and analgesic effects were measured before and repeatedly after drug administration. Repeated-measures ANOVA was used to assess differences among the MINO dose conditions as well as time course.
Results: Preliminary results indicate OXY produced a significant decrease in pupil diameter in comparison to placebo ($p< 0.001$). MINO 100 mg administered in combination with OXY 40 mg reduced ratings of "High" compared to placebo MINO ($p< 0.05$). Both MINO 100 and 200 mg administered in combination with OXY 40 mg reduced ratings of "Good Effect" compared to placebo MINO (both $p< 0.05$). MINO did not alter the physiological effects of OXY.
Conclusions: These preliminary results demonstrate that MINO attenuates the positive subjective effects of OXY in recreational opioid abusers. Future studies should evaluate maintenance treatment with MINO as a potential opioid abuse deterrent agent in opioid dependent individuals.
Financial Support: Financial Support: Supported by DA09236

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CHRONIC MORPHINE ADMINISTRATION AND WITHDRAWAL CAUSE TOLERANCE TO THE SUPPRESSIVE EFFECTS OF MORPHINE ON LPS- INDUCED TNF AND CORTICOSTERONE PRODUCTION IN MICE.

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Aims: To study the differential impact of morphine dependence and withdrawal on Tumor Necrosis Factor (TNF) release and corticosterone production after the intraperitoneal (i.p.) injection of bacterial lipopolysaccharide (LPS) in Swiss Webster (SW) mice.
Methods: Swiss Webster (SW) mice were treated with distinct doses of morphine (0.1-10 mg/kg) applying different schemes of administration. After that, mice received an intraperitoneal injection of LPS (1 mg/kg) and peritoneal washes or collection of trunk blood were performed. Intraperitoneal production of TNF and serum levels of corticosterone after LPS injection was determined utilizing specific ELISA kits.
Results: Morphine administration per se had no effects on basal TNF levels. Morphine inhibited intraperitoneal LPS-induced TNF release but this effect occurred only with high doses (3.1 y 10 mg/kg) and this effect was not dose dependent. Serum corticosterone levels increased after a single LPS challenge and morphine dose dependently prevented this effect. After repeated administration or after morphine withdrawal, tolerance was developed to morphine inhibitory effects on peritoneal TNF release and serum corticosterone levels in response to LPS.
Conclusions: Morphine inhibitory effects on innate immunity depend on the opioid administration schedule and duration treatment.
Financial Support: Supported by Conacyt (grant 188565 to CGE and scholarship 219851 to LMM).

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MODERATING EFFECTS OF RACE IN CLINICAL TRIAL PARTICIPATION AND OUTCOMES AMONG MARIJUANA-DEPENDENT YOUNG ADULTS.

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Aims: Few studies focus specifically on marijuana treatment outcomes among racial minorities. The present secondary analysis of a clinical trial addresses this gap. It was hypothesized that (1) African Americans would have higher attrition rates than Whites, especially during the clinical trial phases following randomization, (2) overall substance use and retention outcomes would vary when stratified by race and (3) race would moderate the relationship between treatment type and outcomes.
Methods: 112 court-referred marijuana-dependent young adults (ages 18-25) were randomized to one of four treatment conditions: Motivational Enhancement Therapy (MET)/Cognitive Behavioral Therapy (CBT), MET/CBT + Contingency Management (CM), Drug Counseling (DC) or DC + CM. African American participants were compared to White participants with respect to rates of participation in phases of treatment and substance use outcomes using chi-square and t-test analyses. In addition, the interaction of race and treatment condition was examined via General Linear Modeling to ascertain if the interventions yielded different effects based on race.
Results: African Americans were significantly less likely to complete the treatment and posttreatment phases of the clinical trial than Whites. Irrespective of treatment type, substance use outcomes did not vary by race. However, there was a significant interaction effect between treatment type and race; African Americans did not benefit differentially from any specific type of treatment, but CM was effective in reducing proportion of marijuana positive samples among White youth.
Conclusions: Findings suggest that clinical trial treatment and posttreatment completion rates vary by race in this population, as does response to treatment. More treatment research focusing specifically on African American marijuana-dependent youth is warranted.
Financial Support: Funding for this study was provided by National Institute of Drug Abuse grants P50-DA009241 and R25-DA020515.

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PATTERNS OF METHAMPHETAMINE USE VARY BY AGE AND HIV SEROSTATUS.

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Aims: Given the high co-occurrence of methamphetamine (MA) use and HIV infection and the aging of HIV persons in the U.S., we examined MA use behaviors in relation to age and HIV serostatus. Considering research indicating possible age-related effects on psychosocial and neuropharmacological factors that may affect MA use patterns, we hypothesized that the oldest cohort may differ in MA use behaviors in comparison to younger cohorts.
Methods: Participants included 227 MA-dependent persons across four 10-year age cohorts (20s: n=22, 30s: n=73, 40s: n=106, 50s: n=26). Individuals underwent extensive substance use, neuropsychological, medical, and psychiatric evaluations. Age cohorts did not differ on demographic factors or prevalence of psychiatric comorbidities, other substance use disorders, or HIV infection.
Results: Analyses of variance revealed significant between-group differences for age of first use, recency of use, and cumulative days of use ($p<.05$). The two youngest cohorts initiated use at a younger age than the next older cohorts, and the oldest cohort reported more remote use than all other cohorts ($ps<.05$). Age and HIV, but not their interaction, significantly predicted age of first use and cumulative days of use ($ps<.0001$). Age, HIV, and their interaction significantly predicted total quantity ($p<.0001$), such that MA consumption increased with advancing age for HIV- ($r=.29$), but not for HIV+ ($r=.02$), persons.
Conclusions: As compared to their younger counterparts, older adults had a later onset, greater duration, and earlier cessation of MA use, which may be driven by psychosocial and/or biomedical factors. In particular, HIV infection appears to dampen the association between older age and greater MA use, perhaps due to incident chronic illness. Older persons without HIV should be assessed for problematic substance use, which may place them at risk for HIV transmission.
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EXECUTIVE FUNCTIONING DEFICITS IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: Cocaine dependence is associated with deficits in executive functioning. Executive dysfunction may be both an etiological factor and a resulting condition of chronic cocaine use. A prerequisite to targeted corrective interventions is a clear understanding of which of the domains of executive functioning are impaired by cocaine-dependence. We hypothesize that all measures of executive functioning will be impaired.
Methods: We compared 79 cocaine-dependent individuals, some of who were also dependent on alcohol, to 61 controls on executive functioning tasks. Each participant completed executive functioning tasks including the Stroop Task, Wisconsin Card Sort Task, Temporal Discounting Task, Conner's Continuous Performance Task, Tower Task, Letter Number Sequence Task, and Iowa Gambling Task. These tasks were chosen to assess a variety of executive functions including cognitive control, cognitive flexibility, attention, self-monitoring, working memory, planning, decision-making, and valuation of the future.
Results: Both cocaine and cocaine and alcohol-dependent individuals performed significantly worse than controls on the executive functioning tasks. The only task that substance-dependent individuals did not perform significantly worse than controls was the Tower Task.
Conclusions: These results provide evidence that cocaine and cocaine and alcohol-dependence are associated with decreased executive functioning across many domains including cognitive control, attention, working memory, decision-making, and valuation of the future. The absence of a significant effect for the Tower Task, an instrument used to assess planning, indicates that the association between cocaine dependence and planning may be weaker than other executive functions. These results support the importance of further study regarding the specifics of which aspects of executive functioning are impaired during substance use as well as inform the design and implementation of executive function therapies.
Financial Support: NIDA and Supplement from NIAAA (R01DA024080)

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PSYCHIATRIC DIAGNOSES AND TREATMENT OUTCOMES IN OPIOID-DEPENDENT INDIVIDUALS RECEIVING BUPRENORPHINE AND BEHAVIORAL TREATMENT.

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Aims: The association between substance use and psychiatric disorders has been well-documented, and comorbidity may predict poorer treatment outcomes. The aim of this study is to examine the prevalence of psychiatric disorders and the association between disorders and treatment outcomes in a sample of opioid-dependent individuals treated with buprenorphine (BUP) and randomized to a behavioral treatment condition.
Methods: This secondary analysis utilizes data collected in a recent study of 202 opioid dependent adults treated with BUP and randomly assigned to 1 of 4 behavioral treatment conditions (cognitive behavioral therapy [CBT], contingency management [CM], CBT+CM, no behavioral treatment [NT]), provided for 16 weeks. To examine the relationship between psychiatric diagnoses and substance use outcomes, psychiatric diagnoses were assessed with the MINI at baseline, and opioid use was assessed using the Treatment Effectiveness Score (TES) which calculates a score using urine drug screens (UDS) collected twice weekly.
Results: A total of 55.0% (N=111) of the sample met DSM-IV criteria for a psychiatric disorder; 25.7% (N=52) for Major Depressive Disorder, 9.4% (N=14) for a psychotic disorder, and 20.8% (N=42) for Antisocial Personality Disorder. The presence of a psychiatric disorder was not associated with opioid use or treatment retention during the behavioral treatment phase. However, medication compliance was greater among participants with a psychiatric diagnosis than those without a diagnosis.
Conclusions: This study included a relatively high prevalence of psychiatric diagnoses among participants, similar to other treatment research. Participants generally improved from baseline to treatment end, suggesting that treatment with buprenorphine in combination with various evidence-based treatment interventions may be successful even if not developed specifically for those with dual diagnoses.
Financial Support: Supported By: National Institute on Drug Abuse (DA020210)

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THEY TRIED TO MAKE ME GO TO REHAB, I SAID, NO, NO, NO: EFFECTS OF LEGAL PRESSURE ON TREATMENT RESPONSE IN A MULTISITE SAMPLE.

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Aims: The effectiveness of drug abuse treatment for clients coerced into care remains controversial. Some studies find legally pressured clients do better than voluntary clients, while others report the exact opposite (Kelley et al, 2005). At the heart of this debate is motivation to change and whether extrinsic pressure to enter treatment impedes personal motivation for change. Opposing views are often fueled by the wide-ranging models that guide delivery of addiction treatment.
The present study examined how participants with and without legal pressure to attend treatment responded to a motivational (MET) vs. traditional (TAU) form of addiction treatment. We hypothesized that MET would be more effective for legally encouraged participants compared with TAU and that effects would be longer lasting for MET.
Methods: NIDA CTN protocol 0004 served as the dataset for this study (Ball et al, 2007). Participants were N=461 clients admitted across 6 outpatient programs. Sample was predominantly male (70.9%) and minority (58%) with mean age 34.8 yrs (SD=10.2). Legal encouragement was defined as "any legal involvement (e.g., probation, mandate) at time of enrollment". A mixed linear model was used to test the effects of legal status (legal involvement, no legal involvement) and treatment group (MET, TAU) across 16 weeks and treatment phase (active intervention, post intervention).
Results: A significant four way interaction was obtained for Treatment Group X Legal Status X Treatment Phase X Time ($F(1,5079.59) = 22.18$, $p < .001$). For legally-motivated clients, drug use declined for both treatment groups, but the largest and most sustained decline was in the MET group. For non-legally motivated clients, drug use increased and was most pronounced in the TAU group.
Conclusions: Findings support a relationship between legal motivation to enter treatment and substance use outcomes. More importantly, the effects appear stronger for clients receiving a motivationally-focused intervention and they persist for up to 3 months post-intervention.
Financial Support: NIH U10 DA 013034

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A NOVEL 5HT2 MODULATOR AS A POTENTIAL ANTIPSYCHOTIC MEDICATION.

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Aims: It is hypothesized that the desired serotonin 5HT2 receptor pharmacology required to treat a variety of disorders is 5HT2A antagonism and/or 5HT2C agonism. Currently, no selective 5HT2A antagonist has demonstrated clinical efficacy to treat these disorders, and a clinically-acceptable 5HT2C agonist that does not also activate 5HT2A (hallucinations) and/or 5HT2B (cardiopulomonary toxicity) receptors has not been reported.
Methods: The (-)-(2S, 4R) and (+)-(2R, 4S) enantiomers of a novel compound, trans-4-(3'-chlorophenyl)-N,N-dimethyl-2-aminotetralin (m-Cl-PAT), were synthesized, and, characterized in vitro for binding and function (activation of PLC/IP formation) at human recombinant 5HT2A, 2B, and 2C receptors expressed in HEK clonal cells. Compounds were administered peripherally (ip) to male C57Bl/6J mice and examined in models predictive of activity to modulate amphetamine-induced behaviors, antipsychotic activity, and in a model of compulsive (binge) eating.
Results: The (-) enantiomer of m-Cl-PAT had approximately 3-, 2- and 20-fold higher affinity than the (+)-enantiomer at 2A, 2B, and 2C receptors respectively, and, was a relatively potent (EC50~300nM) 5HT2C agonist that did not activate 5HT2A or 5HT2B receptors. Both enantiomers attenuated the HTR elicited by DOI, with (-)-m-Cl-PAT being more potent, as predicted by its in vitro pharmacology. The (-)- but not the (+)-enantiomer of m-Cl-PAT completely blocked MK-801-elicited (0.3 mg/kg) and amphetamine-elicited (3.0 mg/kg) increases in locomotor activity. The (-) and (+)-enantiomers of m-Cl-PAT (12 mg/kg) decreased consumption of a highly palatable food in non-food-deprived mice.
Conclusions: The in vitro 5HT2 receptor pharmacological activity of (-)- and (+)-m-Cl-PAT translated in vivo in behavioral studies predictive of efficacy to treat impulsive and compulsive behavioral disorders such as psychostimulant abuse/addiction and binge eating, and to treat psychoses without the adverse side effect of weight gain.
Financial Support: NIH R01 DA030989 and R01 MH081193.

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COGNITIVE INCONSISTENCY IN METHAMPHETAMINE DEPENDENCE IS ASSOCIATED WITH POOR EVERYDAY FUNCTIONING.

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Aims: Methamphetamine (MA) dependent individuals frequently experience daily functioning disruption, and neurocognitive impairment is a clinically-relevant risk factor for such real-world problems. An index of cognitive inconsistency known as intraindividual neurocognitive variability (IIV) shows considerable promise as a sensitive marker of cognitive and functional difficulties, but has not yet been studied in MA-dependent individuals.
Methods: The present study evaluated 35 individuals with recent MA-use disorders (i.e., within 18 months of evaluation) and 55 non-substance dependent comparison (NSC) participants. These groups were clinically well-characterized, and all participants completed a sustained attention task, which yielded summary measures of reaction time and IIV, as well as performance-based measures of everyday functioning outcomes, including instrumental activities of daily living (IADL) and driving (simulator).
Results: A multivariable regression predicting IIV revealed a unique effect of MA-dependence whereby individuals in the MA group demonstrated higher levels of IIV relative to the NSC group ($p = .04$) even when relevant demographic, mood, medical, and cognitive cofactors were controlled. Among MA-dependent individuals, IIV was a significant predictor of IADL and driving outcomes (ps < .05) while accounting for recency of MA use.
Conclusions: These findings suggest that cognitive inconsistency associated with MA-dependence interferes with capacity to successfully perform higher-level, complex daily functions such as IADL and driving. IIV may be a sensitive marker that could identify individuals at risk for failures in other real-world outcomes such as drug treatment compliance and health outcomes.
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USING SERVICE COLLABORATIVES AND IMPLEMENTATION SCIENCE FOR SYSTEM IMPROVEMENT.

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Aims: Significant delays in translating research to practice have led to a research surge in the area of Implementation Science (IS) to determine how to best implement and promote evidence-based practices (EBPs) for youth with complex needs (e.g. co-occurring disorders). In Ontario, Canada, a "Systems Improvement through Service Collaboratives" (SISC) initiative is using IS to improve access to youth mental health and addictions services, service transitions, and health outcomes. Each of 18 regional collaboratives brings together service providers and stakeholders from various sectors (e.g., health, justice, education, aboriginal communities) to collectively identify service gaps and implement system-level changes. Based on an extensive review of existing IS frameworks, SISC has adopted the National Implementation Research Network (NIRN)'s model, which provides a staged-based IS approach with practical EBP implementation-progress evaluation tools. Our evaluation plan, based on developmental evaluation and complex systems analysis, incorporates 1) qualitative approaches (e.g., in-depth case studies); and 2) quantitative approaches focusing on performance indicators both at the provincial-level (e.g., hospital to community transitions) and local level (e.g., school completion rates for aboriginal youth).
Conclusions: For youth with complex needs, there are a myriad of disconnected pathways into mental health and/or addictions treatment. There are also many models for EBP implementation. Our evaluation highlights the benefits and challenges of tracking implementation progress using the NIRN model. Our qualitative approaches demonstrate the importance of local context in both implementation progress and achievement of short-term outcomes. SISC is one of the largest attempts globally to systematically use community partnership to identify systems gaps and implement EBPs across diverse settings. Lessons learned have implications for other large implementation initiatives and could lead to improvement in the experiences of youth with complex needs.
Financial Support: CAMH

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GENDER DIFFERENCES IN CHARACTERISTICS, SERVICE UTILIZATION AND TREATMENT OUTCOMES OF ADULT DRUG TREATMENT COURT CLIENTS.

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Aims: ADTC client needs in relation to health risks, utilization and outcomes are poorly understood. We examined characteristics, health care utilization (chemical dependency treatment, mental health and physical health care) and related treatment outcomes, with a focus on gender patterns.
Methods: Gender comparisons among ADTC clients were examined using Global Appraisal of Individual Need data collected as part of a multi-site collaboration examining drug use, recidivism, service utilization and treatment. ADTC clients who completed two or more follow-ups were included in the analyses (N=199 male, 424 female). Propensity score weights were used to control for size and intake characteristics. Weighted and unweighted comparisons were performed between female and male ADTC clients on measures of treatment need, services received, unmet needs and initial outcomes.
Results: Women were more likely than men to be age 26+, married, to have children under age 21, to report weekly cocaine use and to have higher risk of mental health sequelae from trauma. Women were less likely to graduate high school, to report lifetime or past year substance dependence and to report committing interpersonal crimes. Relatedly, women reported shorter jail stays and more time on probation or parole compared to men. Regarding treatment women were more likely to report depression, moderate or high health problems and multiple prior substance abuse treatment episodes.
Conclusions: Initial findings suggest several distinguishing characteristics of female ADTC clients, with implications for tailored treatment strategies. Women may benefit from augmenting ADTC with more treatment for cocaine abuse, mental health, and physical health needs compared to men to meet their complex needs.
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DISCRIMINATIVE STIMULUS EFFECTS OF A NOVEL EPIBATIDINE ANALOG RTI-102 IN MICE.

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Aims: Developing effective drugs to promote smoking cessation is key to counteracting the potential health risks associated with cigarette smoking. RTI-102 is a low efficacy analog of the high affinity and high efficacy nicotinic acetylcholine receptor agonist epibatidine. To examine its effects in vivo, RTI-102 was studied in a drug discrimination procedure.
Methods: Male C57BL/6J mice (n=8) discriminated nicotine (1 mg/kg, s.c.) from saline while responding under a fixed ratio 10 schedule of food presentation. Nicotine, epibatidine, and RTI-102 were studied alone and RTI-102 was studied in combination with nicotine.
Results: Nicotine and epibatidine both dose-dependently increased nicotine-appropriate responses to a maximum of 86% and 92%, respectively. The ED50 values were 0.86 mg/kg for nicotine and 0.0021 mg/kg for epibatidine. In contrast, RTI-102 could only produce a maximum of 49% nicotine-appropriate responses up to a dose that disrupted responding. When combined with the training dose (1 mg/kg) of nicotine, RTI-102 dose-dependently attenuated the discriminative stimulus effects of nicotine to 33% nicotine-appropriate responding.
Conclusions: The behavioral effects of nicotinic acetylcholine receptor ligands vary as a function of agonist efficacy, as evidenced by the high percentage of nicotine-appropriate responding produced by epibatidine and the lower percentage of nicotine-appropriate responding produced by RTI-102. Further evidence is provided by the antagonism of nicotine by RTI-102 to the level of effect produced by RTI-102 alone. Low efficacy is presumed to be critically important to the effectiveness of some smoking cessation drugs (e.g. varenicline), suggesting that RTI-102 could be developed for the same indication.
Financial Support: Supported by NIH grant DA025267

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SEX DIFFERENCES OF MDMA METABOLISM IN SQUIRREL MONKEYS: A COMPARISON TO FINDINGS IN HUMANS.

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Aims: It was recently reported that women metabolize MDMA differently than men, generating higher MDA and lower HMMA metabolite levels. Notably, there is indication that females may be more prone to a range of effects of substances of abuse, including MDMA. Given the human MDMA use, it is important to understand sex differences that may influence its actions. The present study sought to determine whether sex differences in MDMA metabolism occur in squirrel monkeys, a species that is frequently employed in studies of MDMA-induced neurotoxicity, and that metabolizes MDMA similarly to humans.
Methods: Squirrel monkeys of both sexes (N=6/group) were given single, clinically relevant doses of oral MDMA (0.8 and 1.6 mg/kg). Following treatment, blood was collected at various time points, plasma levels of MDMA and its metabolites were determined, and MDMA pharmacokinetics were calculated. Potential sex differences in MDMA metabolism were explored, and subsequently compared to those previously reported in humans.
Results: As recently reported in humans, female monkeys generated significantly higher (~2.5-fold) peak plasma levels of MDA ($p=0.002$ and $p=0.0002$ at 0.8 mg/kg and 1.6 mg/kg, respectively), and lower levels (~2-fold) of HMMA ($p=0.0004$ and $p<0.0001$ at 0.8 mg/kg and 1.6 mg/kg, respectively), when compared to males. Further, as occurs in humans, animals of both sexes exhibited nonlinear pharmacokinetics indicating inhibition of the CYP2D6 homologue catalyzing MDMA O-demethylenation. Interestingly, female monkeys were more prone to inhibition of MDMA metabolism, as reflected by significantly higher (1.8-fold; $p=0.0051$) disproportionate increases in peak MDMA levels in females than in males with dose increase. This too is in accordance with reports that state faster clearance of drugs metabolized by CYP2D6 in male human subjects.
Conclusions: Squirrel monkeys, like humans, demonstrate sex differences in MDMA pharmacokinetics. These observations provide additional evidence that the squirrel monkey is a useful animal model for predicting (sex specific) outcomes of MDMA exposure in humans.
Financial Support: This work was supported by NIH grants DA05707 and DA01796401

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ASSOCIATION BETWEEN PERCEIVED AND OBJECTIVE MEASURES OF COMMUNITY VIOLENCE EXPOSURE.

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Aims: The purpose of this study was to measure the association between objective measures of residential neighborhood environmental characteristics of violence, alcohol, and other drugs and children's perceived exposure to community violence.
Methods: Data from the Multiple Opportunities to Reach Excellence (MORE) Project was used in this study. The MORE Project is a prospective, observational, 3-year cohort study of the impact of community violence on youth development. The Children's Report of Exposure Community Violence (CREV) was used measure the frequency and level of perceived exposure. Six-hundred and ten children provided data on past year exposure to community violence. The four sub-scales from the Neighborhood Inventory of Environmental Typology (NIfETy) Method were used to measure neighborhood characteristics. Latent profile analysis was used to characterize latent classes of perceived exposure to community violence. Latent class regression was then used to test the association between objective neighborhood characteristics and classes of perceived exposure.
Results: Fit statistics (BIC = 9842.0) indicated that a two class model of perceived exposure provided the best fit. The classes could be distinguished by degree of exposure. None of the four sub-scales of neighborhood characteristics were strongly associated with class membership.
Conclusions: These finding suggest that processes that are more proximal to the child, such as family, peers, school, and individual characteristics, may have a stronger association with children's exposure to violence. These findings do not suggest that objective neighborhood characteristics are not associated with the frequency and degree of exposure children experience. It may be the case that neighborhood factors operate indirectly through other more proximal factors. Further investigation is needed to undercover how neighborhood level processes influence children's experience with violence.
Financial Support: The researcher is supported by a NIDA Drug Dependence and Epidemiology Training Grant (T32DA007292).

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COGNITIVE REGULATION OF CUE-INDUCED CRAVING IN ALCOHOL-DEPENDENT AND SOCIAL DRINKERS.

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Aims: This study aimed to determine whether alcohol dependent drinkers differ from social drinkers with respect to their ability to regulate cue-induced alcohol craving by thinking about the long-term, negative consequences of drinking. We hypothesized that 1) thinking about long-term, negative consequences will reduce cue-induced alcohol craving; and 2) alcohol dependent drinkers will be relatively less capable of this form of cognitive regulation of craving, compared to social drinkers.
Methods: We included 20 non-treatment-seeking alcohol dependent drinkers (AD) and 20 social drinkers (SD), excluding other substance use disorders and other major Axis I disorders. Participants were shown 50 images of alcohol and 50 images of high-calorie foods, with the instruction prior to each image to focus on either the long-term, negative consequences of consuming the depicted substance ("LATER") or the immediate, positive consequences ("NOW"). Stimulus type (ALCOHOL vs. FOOD) and instruction (LATER vs. NOW) were fully counterbalanced within each participant. After each item, participants rated "How much do you want to consume the depicted item?" on a 1-5 Likert scale. Data were analyzed using mixed model ANOVA and post-hoc t-tests.
Results: AD demonstrated an overall higher level of craving for alcohol, compared to SD. There was no difference between ADD and SD with respect to the difference between NOW and LATER instructions.
Conclusions: The results indicate the alcohol dependent drinkers attribute greater motivational salience to alcohol cues, compared to social drinkers, consistent with previous findings. Both alcohol dependent and social drinkers are capable of regulating this motivational salience according to long-term, negative consequences to a similar extent. This suggests that alcohol dependent drinkers may respond to interventions that focus on negative consequences as a way to reduce the motivation to drink.
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EXPLORING TYPOLOGIES OF CRACK USERS AMONG LATINO IMMIGRANT DAY LABORERS IN NEW ORLEANS.

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Aims: Studies indicate crack use among Latino immigrant day laborers (LIDLs) who arrived in New Orleans to work on rebuilding efforts post-Katrina. This emergence of crack use is compelling as it has been previously found to be low among Latinos when compared to other groups and its use has been associated with the spread of HIV and other blood borne pathogens. The aim of this study is to explore heterogeneity among LIDLs who use crack and factors associated to sub-groups of crack users.
Methods: In-depth qualitative interviews were conducted with 52 LIDLs in New Orleans. Participants recruited from day labor sites were: 18 years of age or older; self-reported use of illicit drugs during the past year; arrived in New Orleans post-Katrina; and living in the New Orleans area. In-depth interviews were conducted in Spanish lasting 1–1.5 hrs. Analysis of data consisted of defining the broad dimensions and specific variations distinguishing patterns of crack use.
Results: A post-disaster context, social isolation, workers' rights abuses were identified as contributing factors to drug initiation and periods of daily use. Variations among crack users were seen in frequency of use (occasional users vs. frequent users), initiation of drug use (initiation of drugs pre-migration vs. initiation of drug user post-migration), and family ties (strong ties vs. weak ties).
Conclusions: The emergence of crack use among this sub-group of Latino immigrant day laborers is particularly problematic as this population lacks access to preventative and health care services. Interventions should acknowledge variations in crack use among Latino immigrant day laborers to provide effective services for this vulnerable and high risk population.
Financial Support: NIDA administrative supplement "High Risk Drug and Related Risk Behaviors Among Hispanic Immigrant Workers in New Orleans" National Institute on Drug Abuse (NIDA) $71, 725 [1R01 DA021852-03; PI: Avelardo Valdez]

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FETAL ALCOHOL SPECTRUM DISORDER: A GROWING CONCERN IN ISRAEL?

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Aims: The incidence and prevalence of Fetal Alcohol Spectrum Disorder (FASD) is unknown in Israel. Increasing alcohol consumption countrywide in recent years, lack of awareness of women regarding the toxicity of alcohol during pregnancy, and insufficient knowledge among health professionals (e.g., confusion regarding updated FASD diagnostic criteria), suggest the need to determine national epidemiological patterns of FASD.
Methods: Methods: The first 100 children (under age 2) referred to a newly established national medical adoption unit for medical and developmental assessment, were evaluated for epidemiological and clinical manifestations of FASD. Diagnostic criteria are based on U.S. Institute of Medicine and Canadian Task Force guidelines.
Results: Results: 4 children met FASD criteria – 2 exhibited FAS in the absence of a known history of maternal alcohol exposure, and 2 exhibited partial FAS with confirmed (self-reported) maternal exposure. Another 11 were classified as "highly likely to receive a FASD diagnosis" – 6 with known maternal exposure but no clinical manifestations (ARND - at risk for alcohol-related neurodevelopmental disorder), and 5 with 2 of the 3 FAS criteria but without confirmed maternal exposure.
Conclusions: Conclusions: Based on the high FASD/suspected FASD rate in this high-risk pediatric population, it is estimated that 22-225 FASD "at-risk" babies are born annually in Israel. Others estimate the number to be over 1000. Yet, between 1998 and 2007, only 4 FASD cases were recorded in 17 Israeli hospitals and 6 cases were diagnosed in primary care clinics. It is suspected that the diagnosed cases are only the tip of the FASD iceberg. We hope this report will draw attention to FASD in Israel, increasing public and professional awareness of the impact of alcohol use during pregnancy, develop and increase capacity, create a national framework for screening, diagnosis and reporting and develop evidence-based interventions for prevention, diagnosis and management, and scale up support for FASD research.
Financial Support: Hadassah Medical Organization

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DIFFERENCES IN ILLICIT DRUG USE AMONG MEDICAL, ILLICIT, AND NON-USERS OF MARIJUANA.

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Aims: There is debate about the impact of medical marijuana on the use of illicit substances. While Anderson et al. (2012) found that states with medical marijuana laws reported less cocaine use, the direct relationship between medical marijuana and illicit drug use is unknown.
Methods: We assessed 294 HIV-clinic patients with the ASI-Lite with an additional question on medical marijuana to code patients as "non-users", "illicit users", and "medical users" of marijuana. We compared participants on days of use of heroin, cocaine, and amphetamines based on marijuana use group. When comparing two groups, a correction was applied for performing the three tests (p=0.05/3=0.017).
Results: In the prior 30 days, 163 (55%) participants reported no marijuana use, 44 (15%) reported illicit use, while 87 (30%) reported medical use. Also, 73 (24%) reported amphetamine use, 67 (22%) reported cocaine use and 32 (11%) reported heroin use. Amphetamine use (X^2=21.6, p<0.001), cocaine use (X^2=19.6, p<0.001) and heroin use (X^2=6.6, p=0.037) differed by group. Medical (M=3.4; Z=3.4, p=0.001) and illicit users (M=5.2; Z=4.5, p<0.001) reported more days of amphetamine use than non-users (M=1.2), but medical and illicit users did not differ (Z=1.4, p=0.168). Illicit marijuana users reported more days of cocaine use (M=5.5) than medical users (M=1.9; Z=2.5, p=0.011) and non-users (M=0.9; X^2=4.0, p<0.001), but medical and non-users did not differ (Z=1.4, p=0.165). Medical users (M=2.4) reported more days of heroin use than non-users (M=0.9; Z=2.5, p=0.012), but illicit users (M=1.9) did not differ from medical users (Z=0.6, p=0.579) or non-users (Z=1.4, p=0.149).
Conclusions: Medical, illicit, and non-marijuana users report differing rates of illicit drug use. Medical marijuana users may be at greater risk to use heroin, while illicit users may be more likely to abuse cocaine. Due to the differing rates of other illicit drug use, it may be wise to consider medical and illicit marijuana users as distinct groups in future research.
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SUBSTANCE USE AND HIGH-RISK SEXUAL BEHAVIOR AMONG MEN WHO HAVE SEX WITH MEN IN HANOI.

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Aims: HIV prevalence is increasing among men who have sex with men (MSM) in Vietnam but little is known about their substance use and risky sexual behaviors. We hypothesized that alcohol and illicit drug use is associated with risky sexual behaviors in MSM.
Methods: We conducted a cross-sectional survey in Hanoi in 2010 in MSM recruited through community-based respondent-driven sampling. Participants reported sociodemographic characteristics, alcohol use (AUDIT 8-15=risky, 16-19=harmful, ≥20=dependence), any illicit drug use, and sex without a condom in the past 30 days. We tested associations between substance use and unprotected sex using multivariable logistic regression.
Results: The majority of 451 participants were born outside Hanoi (68.3%), with a mean age of 22.5 (SD 5.3) years. During the past 30 days, 27.1% used illicit drugs, and alcohol use was hazardous for 41.5%, harmful for 23.1%, and consistent with alcohol dependence for 19.3%. Participants had a median 3 sexual partners (range 1-54); 83.1% drank alcohol before or during sexual intercourse and 75.2% reported unprotected sex. In multivariable analysis, age (aOR 0.96, 95% CI 0.91, 0.99), being born outside Hanoi (aOR 1.94, 95% CI 1.14, 3.30), alcohol dependence (aOR 3.34, 95% CI 1.24, 8.98) and alcohol use before or during sexual intercourse (aOR 3.67, 95% CI 1.94, 6.95) were associated with unprotected sex in the past 30 days, but illicit drug use was not (aOR 1.12; 95% CI 0.61, 2.04), after adjusting for education level and income.
Conclusions: Recent alcohol and drug use was common in our sample of Hanoi MSM. Alcohol dependence and drinking prior to sex were associated with unprotected sex, suggesting that tailored interventions to reduce alcohol consumption in MSM may be indicated to reduce behaviors associated with HIV transmission in Hanoi.
Financial Support: Vietnam HIV Addiction Technology Transfer Center (VHATTC) (SAMSHA TI23603); Fulbright Scholar Award 47422223

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METHADONE MAINTENANCE THERAPY IN VIETNAM: AN OVERVIEW AND THE ROLE OF POLICIES FOR SCALING UP.

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Aims: We describe the role of policies for scaling up and sustaining the MMT program in Vietnam
Methods: We use data on patient enrolment in the National Methadone Program to describe the trend of patient and facilities from September 2008 to September 2012. The numbers till 2015 by the MOH is illustrated. We review the effectiveness of the MMT program and summarize the implication of the Decree on sustaining the system of care and treatment for substance abuse disorders and HIV/AIDS in Vietnam. We anticipate key challenges and possible solutions.
Results: From 2008, Methadone treatment program in Vietnam has received strong supports from the Party, Government, and Ministries at all levels. By the end of September 2012, 52 MMT clinics have been opened, providing Methadone treatment for 10,600 patients. Besides, patients receive variety of auxiliary services including counseling, accessing clean syringes and needles, condom, peer education, group and family meetings, HIV counseling testing, referral to Anti Retro Viral Treatment (ARV) and other treatments when needed. Studies have showed positive outcomes around health, social and economic aspects. MOH has aimed to have 67 MMT clinics and treat 15,600 patients in 13 provinces by the end of 2012. Nationally, around 80,000 patients will be treated in 245 clinics by 2015. The MMT Decree, the enormous effort led the MOH in collaboration with relevant government ministries creates needed framework and terms for increasing access, expanding program, ensuring the sustainability and quality.
Conclusions: The Decree approved in November 14, 2012 supports the collaboration and coordination in the implementation of the effective and sustained national MMT program. It helps maximize the use of resources for the prevention, care and treatment of both HIV/AIDS and opioid dependence.
Financial Support: No financial support has been identified

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PRECLINICAL EVALUATION OF JPC-077 AS A NOVEL TREATMENT FOR METHAMPHETAMINE ABUSE.

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Aims: Methamphetamine (METH) abuse continues to be a health care burden. Lobeline, an alkaloidal constituent of *Lobelia inflata*, has efficacy in attenuating reward induced by METH, primarily via interaction with the vesicular monoamine transporter-2 (VMAT2). Lobeline also inhibits nicotinic receptors, revealing a lack of selectivity at VMAT2. Chemical defunctionalization of lobeline afforded lobelane, which demonstrated improved VMAT2 selectivity. The current study provides preclinical data in support of a novel lead analog of lobelane, JPC-077, as a treatment for METH abuse.
Methods: The effects of JPC-077 at VMAT2 and the dopamine transporter (DAT), and as an inhibitor of METH in slice preparations, were evaluated. Also, translation to the whole animal was pursued by determining JPC-077-mediated inhibition of responding for METH in self-administration assays.
Results: Results show that JPC-077 exhibited a 6-fold increase in affinity for the [^{3}H]dihydrotetrabenazine binding site on VMAT2, and a 5-fold increase in affinity for the dopamine (DA) translocation site on VMAT2 in relation to lobelane, as well as a competitive inhibition of DA uptake at VMAT2. JPC-077 evoked [^{3}H]DA release from synaptic vesicles with 130-fold greater potency than lobelane or METH. JPC-077 had 370-fold greater selectivity for VMAT2 over the plasmalemma DAT, indicating that JPC-077 likely has low abuse liability. Importantly, JPC-077 inhibited METH-evoked DA release from striatal slices, while concurrently increasing extracellular DOPAC. JPC-077 (56 mg/kg) decreased the number of methamphetamine infusions self-administered, but did not alter responding for food when given across repeated pretreatments.
Conclusions: Thus, in vitro effects of JPC-077 translated to in vivo efficacy, decreasing METH self-administration. As a result of these studies, JPC-077 has emerged as a lead compound in the development of a treatment of METH abuse.
Financial Support: DA13519, DA016176, TR000117

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DYNAMIC MODELING OF INITIATION OF NONMEDICAL OPIOID USE.

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Aims: Drawing from empirical data and a panel of experts, a system dynamics simulation was developed to reproduce historical trends in nonmedical use of pharmaceutical opioids. System dynamics is a simulation method in which complex relationships and feedback loops are specified and mathematically formalized. The resultant set of differential equations was calibrated to replicate data from 1995-2005, used to predict behavior from 2006-2011, and used to evaluate policy interventions.
Methods: Data to support assumptions and model parameters were drawn from publicly available sources. Data on initiation and nonmedical use were obtained from the National Survey of Drug Use and Health for 1995-2011.
Results: The model contains 5 state variables, 13 exogenous parameter variables, 21 calculated parameters and 10 rates of change. Three principal feedback loops (a peer initiation epidemic loop, a global availability loop, and a personal accessibility loop) contribute to the nonlinear growth patterns in nonmedical opioid initiation and use. Peer initiation is modeled as the infection of a susceptible population by peers. Global availability of opioids for nonmedical use depends on the number of current opioid users and how much free leftover medicine they obtain from prescription holders. When availability diminishes, reduced personal accessibility requires transitions to paying for opioids. A demand-side intervention appeared to be more effective than constraining supply; compelling susceptible non-users to resist initiation was more effective in reducing nonmedical use than compelling prescription holders not to share their medicines, and reducing global availability through prescription take back events.
Conclusions: We offer a formalized model of a common pathway to nonmedical opioid initiation and provide a tool for comparing the impact of multiple policy interventions. System dynamics modeling sheds insights on the global dynamics of nonmedical opioid use and can be used to inform policy interventions to ameliorate the associated public health problems.
Financial Support: NIDA grant 5R21DA031361.

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GENETIC VARIANTS OF THE DOPAMINERGIC SYSTEM ASSOCIATED WITH SUBJECTIVE RESPONSES TO COCAINE.

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Aims: To identify genetic markers of the dopaminergic system that modulate subjective responses to cocaine in cocaine-dependent subjects.
Methods: Non-treatment seeking cocaine-dependent subjects (N = 47) received in randomized order a single infusion of saline or cocaine (40 mg, IV) delivered over a 2 min period. Subjective effects (visual analogue scales: VAS) were acquired before (-15 min) and at 5, 10, 15, and 20 min after infusion. VAS scales ranged from zero (no effect) to 100 (greatest effect ever). Subjective values following cocaine were normalized to baseline values collected 15 min prior to each infusion, and then were subtracted from saline session values. Data was analyzed using repeated measures ANOVA. DNA from subjects was genotyped for the *DRD2* rs6277 and rs2283265, *ANKK1* rs1800497, and *CSNK1E* rs1534891 variants. Results were corrected for population structure.
Results: Our cohort had a mean age of 44 years, was 68% black, 87% male, and primarily smoked >2 g cocaine per day (94%). Self-report of "High" and "Any Drug Effect" were found to be in association with *DRD2* (rs2283265: $p = 1x10^{-3}$, $p = 3x10^{-4}$, respectively), and *ANKK1* ($p = 6x10^{-5}$, $p = 3x10^{-4}$) variants. Associations were found with reports of "Like Cocaine" with *ANKK1* ($p = 4x10^{-4}$) and "Anxious" with *CSNK1E* ($p = 7x10^{-4}$).
Conclusions: This study provides evidence that inter-individual differences in genetic makeup modify subjective responses to cocaine. Knowledge of the genes and variants that modulate response to cocaine may aid in the development of novel therapies for the treatment of cocaine addiction.
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IS PAIN ASSOCIATED WITH ILLICIT OPIOID USE OR ABERRANT OPIOID-RELATED BEHAVIORS IN OPIOID SUBSTITUTION TREATMENT PATIENTS.

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Aims: The limited literature on pain in opioid treatment samples indicates that current pain is highly prevalent. Understanding the clinical implications of current pain on treatment outcomes is important, particularly in light of ageing opioid treatment cohorts. This study aims to explore correlates of pain, including aberrant behaviors related to prescribed opioid use.
Methods: Data on pain, physical health and previous tried pain treatments were collected in methadone or buprenorphine patients (n = 141) from three treatment services. Measures included basic demographics, the Brief Pain Inventory, measures of general mental and physical health and quality of life questions, pain history and previous treatments tried for pain. Univariate and multivariate analysis were used to examine correlates of pain.
Results: Forty percent of the sample reported current pain. Of those with current pain, 68% reported trying some form of treatment other than prescribed opioids. Correlates of current pain were depression, anxiety and poorer ratings of health. Current pain was not associated with greater use of illicit opioids (prescribed opioids or heroin) nor with any aberrant opioid related behaviors. Pain levels were comparable amongst methadone and buprenorphine treatment participants.
Conclusions: The high prevalence of severe mental health comorbidity amongst opioid dependent people with current pain suggests screening for pain and tailoring of treatment where pain exists is warranted. The lack of association with pain and aberrant behaviors suggests it should not be assumed that those in opioid treatment misuse medications in response to pain.
Financial Support: Funding for the parent study was provided by Reckitt Benkiser in the form of an united educational grant; the funders had no role in study design; in the collection, analysis and interpretation of data; or in the decision to submit the paper for for presentation at CPDD.

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DIFFERENT SENSITIVITY FOR OXYCODONE-INDUCED CONDITIONED PLACE PREFERENCE AND SENSITIZATION OF LOCOMOTOR ACTIVITY IN ADOLESCENT AND ADULT MICE.

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Aims: Nonmedical use of the prescription pain reliever oxycodone has become a major public health issue in the United State, especially among adolescents. Although adults and adolescents have different sensitivity for the drug, little is known about the rewarding and locomotor stimulating effect of oxycodone in adolescents compared to adults. Here, we investigate the sensitivity to the rewarding effect of oxycodone and to the effect on locomotor activity in adolescent (4 weeks old) and adult (10 weeks old) C57BL/6J mice using conditioned place preference paradigm.
Methods: The pre-test was conducted before the drug exposure. During conditioning sessions, mice were confined to one compartment for 30 min after oxycodone (0, 0.3, 1, 3 mg/kg, i.p.) or to the other compartment after saline injection. The mice were injected with oxycodone and saline on alternate sessions, for a total of eight conditioning sessions with four oxycodone and four saline trials for each animal. The day after the last conditioning session, the post-conditioning test session was performed. During the conditioning sessions, locomotor activity was assessed as the number of "crossovers" defined as breaking the beams at either end of conditioning compartment.
Results: Adult mice developed conditioned preference at all three doses (0.3, 1 and 3 mg/kg) of oxycodone. However, adolescent mice developed conditioned preference at the two higher doses (1 and 3 mg/kg), but not the lowest dose (0.3 mg/kg), of oxycodone. Adult mice developed sensitization of locomotor activity at only the highest doses (3 mg/kg) of oxycodone. However, adolescent mice developed sensitization of locomotor activity at the two higher doses (1 and 3 mg/kg) of oxycodone.
Conclusions: These findings suggest that while adolescents may need higher doses of oxycodone to get the same rewarding effect as adults, adolescents may be more readily sensitized to oxycodone.
Financial Support: NIH-NIDA 1RO1DA029147-01A1 (YZ) and NIH-NIDA P60DA05130 (MJK).

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EFFICACY OF BRIEF TREATMENT FOR ECSTASY USE.

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Aims: To test the hypothesis that three sessions of motivational enhancement and cognitive behavioural therapy (e Check-up Plus) would reduce ecstasy use more so than one session of motivational enhancement therapy alone (e Check-up).
Methods: 54 individuals (males = 38; M age = 26.20 years, SD = 9.49) were randomized to either the e Check-up Plus (n = 27) or the e Check-up (n = 27). Individuals who were randomized to the e Check-up received one 50-minute session of motivational enhancement therapy, whereas individuals randomized to the e Check-up Plus received the motivational enhancement session plus 2, 50-minute sessions of cognitive behavioral therapy devoted to conducting a functional analysis of participants' ecstasy use and using this information to devise strategies for managing ecstasy use. Participants were non-treatment seeking individuals with low motivation to change their use (M URICA score = 5.91; SD = 2.72). As such, the study was advertised as a nonconfrontional opportunity to discuss one's ecstasy use. Participants' ecstasy use was monitored at baseline, and at 4-, 16-, and 24-weeks post baseline.
Results: Multivariate tests did not show a statistically significant time by treatment condition effect, Wilks lambda = 0.99, $F(3, 45) = 0.21$, $p = 0.88$; however, there was a statistically significant time effect, Wilks lambda = 0.48, $F(3, 45) = 16.56$, $p < 0.001$. Paired-samples t tests demonstrated that participants used fewer ecstasy pills per month at the 4-week follow-up (M =2.64; SD = 3.67) compared to at baseline (M =5.65; SD = 4.04; $t(52) = 5.27$, $p < 0.001$, and that this reduction was maintained at the 16-week (M =2.14; SD = 2.62; $t(50) = 7.14$, $p < 0.001$) and 24-week follow-up (M =2.14; SD = 2.94; $t(48) = 7.02$, $p < 0.001$).
Conclusions: On average, participants reduced their ecstasy use by 62% from baseline to the 24-week follow-up. The treatments were found to be statistically equivalent, and thus, a one-session motivational intervention may be sufficient for substantially reducing unmotivated, non-treatment seeking individuals use of ecstasy.
Financial Support: Australian Government Department of Health and Ageing under the National Psychostimulants Initiative.

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WOMEN AND ENTRY TO RESIDENTIAL DETOXIFICATION TREATMENT: MOTIVATIONS AND BARRIERS.

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Aims: A much smaller number of Iranian women participate in drug use treatment programs compared with their male counterparts because of stigma and the male-dominated drug use treatment settings. The aim of this study was to explore Iranian women`s motivations and barriers to enter residential detoxification treatment.
Methods: A qualitative study using in depth-interviews was conducted. The study was conducted in 2009 and included 80 female drug users at the largest female-specific residential detoxification center in Tehran, Iran. Recruitment was continued until data saturation occurred. The grounded theory approach of Strauss and Corbin was applied to code and analyze the data.
Results: The mean age of the sample was 34 (SD=7) years. 54% were married. 29% were single. 48% had some elementary education. 41% had some high school education, and 65% were jobless. 62.9% were heroin smokers. 30.8% were coabusers of heroin and methamphetamine. Mean duration of drug use was 9 (SD=5.1) years. 12-step meetings, group therapy, supportive role of female peers in treatment, female-specific setting of treatment, free-drug setting of residence, and lack of using chemical medicines for treatment were the most important facilitators for treatment entry while fear from experiencing withdrawal symptoms, separation from family especially children, fear from being stigmatized by relatives and friends, and long duration of residence were known as their most common barriers for entry to treatment.
Conclusions: The motivations and barriers associated with entry to residential detoxification treatment which were revealed in this study have not been addressed by residential detoxification treatment program for women in Iran. Considering such factors could contribute to better treatment entry by Iranian drug-using women
Financial Support: No financial support was received.

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OPIOID SUBSTITUTION TREATMENT ENROLLMENT AND OUTCOMES IN CALIFORNIA:1991-2011.

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Aims: To provide a descriptive analysis of the opioid substitution treatment (OST) delivery system, we examine trends in demographic and drug use characteristics of patients accessing OST in California over the past 20 years.
Methods: Statewide administrative data was obtained from the California Alcohol & Drug Data System (CADDS;1991-2005) and California Outcome Measurement System (CalOMS;2006-2011) on all patients admitted to publicly-funded OST programs from 1991 to 2011. Univariate trends in demographic, drug use characteristics and treatment outcomes were considered. Cochran-Armitage tests were applied to confirm observed trends.
Results: The study sample consisted of 240,225 individuals and 689,192 treatment episodes. Individuals had a median 2(IQR:1-5) OST episodes during the study period. The annual number of new OST admissions peaked in 1994 (51,902) and fell to 18,480 in 2011; within these years, detoxification treatment admissions fell from 88.0% to 41.4%($p<0.01$). Overall, rates of retention in treatment at 3 and 12 months during the study period were 32.2% and 18.1%, respectively; among maintenance-oriented treatment admissions, these rates were 70.5% and 44.1%. Among client characteristics, prescribed opioids have been more frequently reported as the primary drug of abuse in recent years, reaching 24.0% of all admissions in 2011; injection as the primary route of administration has subsequently fallen to 62.0% in 2011 from a high of 94.8% in 1992. The proportion of admissions by individuals aged 25 and under has increased from 15.9% in 2003 to 31.7% in 2011($p<0.01$). Finally, rates of Hepatitis C Virus and HIV testing were relatively constant at 24% and 70%, respectively, from 2006-2011.
Conclusions: Both the mode of OST delivery and client demographics have shifted substantially in California over the past 20 years. Monitoring and evaluation efforts are necessary to inform health system innovation and reform.
Financial Support: NIDA grant no.R01DA031727(PI:Nosyk)

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EVALUATION OF OPIOID WITHDRAWAL AFTER MAINTENANCE ON EXTENDED-RELEASE TRAMADOL.

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Aims: The aim was to evaluate whether abrupt cessation of dosing with extended-release (ER) tramadol produced evidence of opioid withdrawal.
Methods: This was an inpatient, double blind, randomized, three-arm, placebo-controlled trial. Key eligibility criteria included: age 18-55 years old, short-acting prescription opioid use > 20 of the last 30 days, and meeting DSM-IV criteria for current opioid dependence with observed withdrawal. After random assignment to ER tramadol (0, 100 or 300 mg bid for 7 days; n=12/group), all groups crossed over to placebo for 6 additional days of monitoring. Four breakthrough withdrawal medications were available. Primary outcomes were: 1) number of breakthrough withdrawal medication doses taken, and 2) subject-rated opioid withdrawal. Secondary outcomes included observer-rated withdrawal ratings, physiologic and cognitive measures, and serious adverse events.
Results: Amount of breakthrough withdrawal medication differed significantly among groups ($p<0.001$) over the 6-day placebo-dosing period whereby the 600 mg tramadol group requested significantly more rescue doses on days 2-4 (Dunnet $p<0.05$) versus the placebo-assigned group. Specifically, more acetaminophen was used in the 600 mg transfer group than placebo on days 2-4 (Dunnet $p<0.05$). There were no statistically significant increases on subject-rated withdrawal measures. Observer-rated withdrawal scores for the 600 mg group increased modestly from days 2 to 3 and then decreased to values similar to the 200 mg and placebo groups. There were no serious adverse events.
Conclusions: Abrupt cessation of repeated dosing with ER tramadol 600, but not 200 mg, produced opioid withdrawal as evidenced primarily by increased use of rescue medications.
Financial Support: NIDA R01 DA027068 (MRL), T32 DA007304 and NCRR and NCATS UL1RR033173.

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PREVALENCE OF HIV, HEPATITIS C AND DEPRESSION AMONG PEOPLE WHO INJECT DRUGS IN THE KINONDONI MUNICIPALITY IN DAR ES SALAAM, TANZANIA.

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Aims: The aim of this study was to determine the HIV and hepatitis C seroprevalence among people who inject drugs in the Kinondoni Municipality of Dar es Salaam, Tanzania. In addition, we sought to examine the prevalence of depression among this population.
Methods: We conducted a cross-sectional study examining known HIV/HCV risk behaviors and a screen for depression. Subjects were tested for HIV and HCV antibodies using rapid ELISA assays. The study was conducted over a period of six months from November 2010 to April 2011 among PWID who attended community outreach services throughout the municipality.
Results: 419 PWID were recruited and 76.6% (n=321) were male and 23.4 % (n= 98) were female. The mean age was 26.6 years (range 18 to 53). Sixty four percent of patients (n=269) were 25 to 34, while less than 1% were older than 45. The cumulative prevalence of HIV and HCV positive antibody status among PWID was 51.1% and 75.6%, respectively. The prevalence of depression was lower at 19.3%. Clear gender disparities existed between male and female PWID, with women having a greater prevalence of HIV, HCV and depression than men.
Conclusions: An investment in the expansion of HIV/HCV prevention services including the establishment of large-scale needle-syringe programs and the rapid expansion of low threshold, high volume methadone clinics to additional areas of Dar es Salaam remains a priority. Of particular importance will be targeting female injectors who are disproportionately affected by HIV, HCV and depression.
Financial Support: Departmental funding of the Muhimbili University of Health and Allied Sciences was utilized for this study.

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ANTIRETROVIRAL MEDICATION DIVERSION IN SOUTH FLORIDA: PRESCRIPTION TYPES AND MOTIVATIONS.

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Aims: News reports and qualitative data have pointed toward the emerging phenomenon of ARV diversion by HIV positive individuals. However, studies documenting commonly diverted medications, diversion motivations and medication recipients are lacking. We examined these factors in an exploratory south Florida study.
Methods: Respondents were at least 18 yrs of age (mean = 46), confirmed HIV positive, prescribed ARV medications, and 12 or more occasions of cocaine or heroin use in the last 3 months. Those who had recently diverted ARV medications were included in this analysis (n=251). Trained interviewers administered standardized assessments that included detailed lifetime and current drug use, as well as history of HIV infection and treatment. Participants were first diagnosed with HIV an average of 12.7 years and were first prescribed HIV medications an average of 9.8 years prior to interview. The participants first began selling their prescription HIV medications an average of 2.8 years prior to interview, and had sold or traded them a median of 7 times.
Results: Our findings indicate a variety of diverted HIV medications. The most frequently diverted medications (past 3 months) included Atripla® (diverted by 31.9% of the participants), Norvir® (29.5%), and Truvada® (39.8%). A majority recently sold/ traded their HIV medications for money for drugs or alcohol (72.5%). Medications were sold to pill brokers 79.7% of the time, and to another HIV-positive person for their use 11.6% of the time. The diverters knew, on average, 4 other people who were involved in selling ARV medications.
Conclusions: Findings demonstrate that many substance users have histories of HIV medication diversion related to their alcohol and drug use. The sale or trading of ARVs reduces adherence, reducing treatment effectiveness and increasing viral load. Given this, further study is warranted to explore risk factors for diversion, and develop interventions to reduce the diversion by this vulnerable population of these needed medications.
Financial Support: This work was supported by NIH Grant R01DA023157.

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CHILDHOOD STRESSORS DIFFERENTIALLY AFFECT AGE OF FIRST USE AND TELESCOPING ACROSS WOMEN AND MEN.

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Aims: Prior work has documented that the experience of childhood stressors decreases age of first use and shortens the length of time from first use to dependence (i.e., telescoping) for illicit drugs, alcohol, and tobacco. However, it is currently unknown whether the experience of childhood stressors on age of first use and telescoping differ across men and women.
Methods: Analyses were conducted with NIAAA's National Epidemiologic Survey on Alcohol and Related Conditions (n=34,653, age 18+). Outcome variables included: age of first substance use (illicit drug, alcohol, and tobacco), age of onset of DSM-IV dependence diagnosis (illicit drug, alcohol), onset of daily tobacco use, and telescoping (age of onset of dependence minus age of first use). Predictor variables included: gender and total number of childhood stressors (i.e., physical, sexual, and emotional abuse, family violence, and neglect). Regression analyses were conducted.
Results: Results demonstrated a consistent pattern across illicit drug, alcohol, and tobacco use, but differed age cohorts (i.e., not all age cohorts demonstrated significant effects for all substances). Men who were exposed to a higher number of childhood stressors initiated use at a younger age than women. Women who were exposed to a higher number of childhood stressors had more rapid telescoping than compared to men. There were minimal gender differences in age of first use or telescoping among those with fewer childhood stressors.
Conclusions: Using a large nationally representative dataset, this is the first study to document that the effect of childhood stressors on age of first use and the length of time to transition to dependence differed across women and men. Knowledge such as this is essential to develop age-appropriate and gender-sensitive prevention strategies.
Financial Support: The National Institute on Health 5T32DA007238-22 (Petrakis), P50DA033945 (ORWH and NIDA; McKee)

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ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ADVERSELY IMPACTS EVERYDAY FUNCTIONING IN CHRONIC METHAMPHETAMINE USERS.

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Aims: Methamphetamine (MA) use commonly accompanied by significant clinical disabilities, the severity which is associated with neurocognitive impairment, polysubstance use, and psychiatric comorbidity (e.g., depression). One previously unstudied psychiatric comorbidity that may be particularly relevant to real-world functional outcomes among MA users is Attention-Deficit/Hyperactivity Disorder (ADHD), which is independently associated with a wide range of problems in everyday functioning.
Methods: In the current study, we evaluated 400 individuals with DSM-IV diagnoses of MA use disorders within 18 months of evaluation who completed a comprehensive neuropsychiatric and medical research battery. 21% (n=83) of the MA subjects met lifetime diagnostic criteria for ADHD (13% with current diagnoses) as determined by structured clinical interview. All participants completed self-report measures of everyday functioning, including declines in instrumental activities of daily living (IADL), cognitive complaints, and employment status.
Results: Separate regressions predicting the three everyday functioning outcomes from ADHD group, along with important co-factors (i.e., demographics, depression, other substance use disorders, and recency of MA use) were significant at the omnibus level (ps < .01). Examination of individual predictors in these models revealed that ADHD diagnoses were uniquely associated with greater concurrent risk of declines in IADL, elevated cognitive complaints, and unemployment (ps < .01).
Conclusions: Findings indicate that ADHD may play an important role in MA-associated disability in a wide range of real-world activities, which may reflect increased comorbidity burden on neurocognitive abilties, premorbid risk factors, and/or psychosocial competencies in already vulnerable chronic MA users. Efforts to screen for and treat ADHD in individuals with MA dependence may help to improve real-world outcomes.
Financial Support: This research was supported by National Institutes of Health grants P01DA12065, P50DA026306, T32DA031098 and P30MH62512.

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SUBSECOND DOPAMINE RELEASE IN CANNABINOID TOLERANCE.

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Aims: Cannabinoids, including marijuana and its synthetic analogues, are the most frequently abused class of illicit drugs in the United States. The brain's mesolimbic dopamine system is thought to mediate the rewarding/reinforcing properties of all drugs of abuse, including cannabinoids. Although repeated cannabinoid exposure is known to produce tolerance to several behavioral and physiological measures, it remains unclear whether such a pharmacological history also produces tolerance to its dopamine releasing effects.
Methods: Rats were treated with either vehicle or a synthetic cannabinoid (WIN55-212-2; WIN) using an escalating dosing approach (0.2-0.8 mg/kg IV over 9 treatments). We then assessed whether this dosing regimen produced tolerance to a series of behavioral/physiological measures that are routinely observed when rodents are treated with WIN (i.e., tetrad test: catalepsy, hypothermia, antinociception, and spontaneous activity). Finally, we used fast-scan cyclic voltammetry to measure real-time WIN-evoked dopamine release in the nucleus accumbens in freely-moving and behaving rats.
Results: WIN-treated rats showed a rightward dose effect curve shift (0.002-0.8 mg/kg IV) in each behavioral/physiological measure versus vehicle treated controls. Likewise, the dopamine releasing potency of WIN was significantly reduced in the WIN-treated rats when tested at the 0.2 mg/kg IV dose.
Conclusions: These results demonstrate that subchronic administration of the synthetic cannabinoid WIN can produce tolerance to its dopamine releasing effects. A diminished ability to increase dopamine release may contribute to the abuse of larger cannabinoid doses and quantities, thereby advancing the addiction process.
Financial Support: Funded by NIDA grants: R01DA015718, R01DA022340, R01DA025890, R21DA033926 (JFC); F32DA032266 (EBO).

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MEDIATORS OF RESPONSE TO SERTRALINE VS. PLACEBO AMONG RECENTLY ABSTINENT, COCAINE-DEPENDENT PATIENTS.

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Aims: In order to optimize treatment outcomes with the DA reuptake inhibitor sertraline (SERT), data from two 12-wk, randomized, double blind, placebo-controlled clinical trials of SERT for preventing relapse among recently abstinent, cocaine dependent patients (N=126) were analyzed to determine mediators of treatment response.
Methods: Participants resided at a residential treatment facility (wks 1-2) and randomized to receive either SERT alone (200 mg/day) or placebo. Participants transferred to outpatient treatment at the start of their third week, continued to receive study medications or placebo (weeks 3-12) and participated in weekly individual cognitive behavioral therapy. Compliance with study protocol was facilitated by providing monetary compensation for attendance and for returning blister packs. Supervised urines were obtained thrice weekly. The primary outcome was relapse (i.e., 2 consecutive urines positive for cocaine).
Results: Logistic regression showed the odds ratio (OR) of the SERT group vs. the placebo group to be 0.64($p<0.0001$), making SERT-treated subjects significantly less likely to relapse than placebo subjects. The model also adjusted for several other covariates including: gender, age, current alcohol dependence diagnosis (ADD) and the interaction of treatment group and current ADD. Women were less likely to relapse than men (OR=0.45, $p<0.0001$). Older subjects were more likely to relapse than younger subjects (OR=1.06, $p=0.02$). ADD subjects were more likely to relapse than those who were not dependent (OR=3.45, $p=0.0002$). However, the ADD effect was moderated in SERT-treated subjects by the interaction term (OR=0.30, $p=0.0004$).
Conclusions: Thus, participants who are women or younger may have better outcomes in a relapse model regardless of treatment. In addition, outcomes in ADD participants were more negative than non-ADD participants when receiving placebo, but not SERT. Overall, the results suggest that SERT improves outcomes relative to placebo, especially in those with comorbid ADD.
Financial Support: Supported by NIDA grant P50 DA12762

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CUANDO TOMO MAS, SIENTO QUE ES UN REFUGIO: CONTEXT OF ALCOHOL USE AMONG LATINO IMMIGRANT MEN.

India Ornelas[1], C Allen[1], C Vaughan[1], Nalini Negi[2], E Williams[1]; [1]Health Services, University of Washington, Seattle, WA, [2]Social Work, University of Maryland, Baltimore, MD

Aims: Latino immigrant men face many difficulties in adapting to life in the United States, and previous studies suggest that heavy alcohol use is one coping mechanism in response. The aim of this study was to understand the the context of alcohol use among Latino immigrant men as a basis for developing interventions to reduce heavy alcohol use in this population.
Methods: Latino immigrant men (N = 27) who were current drinkers were recruited from community-based organizations to participate in focus groups and semi-structured 1:1 interviews. Data were collected in Spanish by trained bilingual research staff. Recordings were transcribed, then transcripts were coded and analyzed in Atlas.ti. Case summaries and coded quotations were reviewed for to identify themes.
Results: Patterns of alcohol use included frequent drinking which often occurred daily or several times a week. Binge drinking was also common. Most men chose to drink at home or in "hidden" public areas where they would not be seen by authorities. Men were more likely to drink when feeling lonely, social isolated, and guilty about being away from their families. Drinking also helped men feel more strong, confident, friendly and conversational. Negative consequences of drinking included debt, poor work performance, or job loss. Aggression and violence were also commonly described negative consequences which negatively influenced their family relationships. Some men reported wanting to decrease their drinking, but did not have support in their social networks and primarily coped with problems alone. Many knew about Alcoholics Anonymous, but did not feel comfortable going to meetings.
Conclusions: Unhealthy drinking and negative consequences were common among this convenience sample of Latino immigrant men. As such, community based screening and intervention may help reduce heavy alcohol use in this vulnerable population.
Financial Support: This project was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Number KL2TR000421.

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METHADONE AND SUBOXONE® FOR SUBUTEX® INJECTORS: PRIMARY OUTCOMES OF PILOT RCT.

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Aims: Aims Determine the extent to which buprenorphine (Subutex®) injectors accept treatment with buprenorphine-naloxone (Suboxone®) or methadone, and the impact of these treatments on HIV risk and injecting use in the Republic of Georgia.
Methods: Design Randomized controlled 12-week trial of daily-observed methadone or buprenorphine-naloxone.
Setting Uranti clinic in Tbilisi, Republic of Georgia,
Participants 80 consenting treatment-seeking individuals (40/group) aged 25 and above who met ICD-10 criteria for opioid dependence with physiologic features and reported injecting buprenorphine 10 or more times in the past 30 days.
Measurements: Opioid use according to urine tests and self-reports, treatment retention, and HIV risk behavior as determined by the Risk Assessment Battery.
Results: Results: Mean age of participants was 33.7 (SD5.7), 4 were female, mean history of opioid injection use was 5.77 years (SD4.6), none were HIV+ at intake and at 12-week assessment, and 73.4% were HCV+. Of the 80 patients, 68 (85%) completed the 12-week study treatment and 37 (46%) were in treatment at the 20-week follow-up. In both study arms treatment participation resulted in a marked reduction in unprescribed buprenorphine and other opioids use and HIV injecting risk behavior. There were no significant differences in outcomes between the two treatments. Medications were well tolerated and no serious adverse events were reported.
Conclusions: Conclusions Daily observed methadone or buprenorphine-naloxone are effective treatments for non-medical buprenorphine and other opioid use in the Republic of Georgia, and likely to be useful for preventing HIV infection.
Financial Support: NIDA R21-DA-026754

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CIGARETTE SMOKING AMONG A SAMPLE OF URBAN, CURRENT AND FORMER SUBSTANCE-USING, PERSONS LIVING WITH HIV/AIDS.

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Aims: To explore the associations between social environmental and individual-level characteristics with current cigarette smoking among a sample of urban, current and former drug users among persons living with HIV/AIDS (PLHAs).
Methods: Data for these analyses came from the BEACON study, a NIDA-funded longitudinal study aimed at examining social environmental (i.e., support network and informal care giving) influences on former and current drug users' HIV medication adherence and health outcomes. Data came from the 6-month visit, and the sample included 358 individuals. Descriptive statistics and logistic regression analyses were used to describe the associations.
Results: The majority of the sample reported being current cigarette smokers (75%) and almost half of the sample reported current drug use (45%). In the adjusted analyses, recent drug use (OR=2.82, 95% CI=1.55-5.13) as well as having a main supporter who is a current smoker (OR=2.01, 95% CI=1.14-3.54) were significantly associated with current cigarette smoking.
Conclusions: In this sample of urban, HIV-positive individuals who are current or former substance users, both individual-level and social-level factors were associated with current cigarette smoking. These findings have implications for the development of targeted smoking cessation interventions for PLHAs.
Financial Support: This work was supported by F31 DA033873 (Pacek), R01 DA032217-02S1 (Latkin), and R01 DA019413 (Knowlton).

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UNDERSTANDING MODULE EFFECTS IN OPEN-ENROLLMENT GROUP THERAPY STUDIES.

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Aims: It is not known how the content of group therapy sessions may be related to client symptom reporting. We examine whether session theme, or module, moderates changes in symptoms reported during treatment, while accounting for correlation of session-level moderators and random session effects to avoid variance inflation that may result in falsely significant findings.
Methods: Clients with moderate levels of depressive symptoms upon treatment entry who participated in a group cognitive behavioral therapy (GCBT) intervention. N=132 residential clients participated in a four-module GCBT. N=44 outpatient clients participated in a three-module GCBT. PHQ-9 depressive symptoms scores were collected from clients as they attended sessions. A growth model was fit to PHQ-9 scores assessed at two-week intervals during treatment. Time since GCBT entry and module theme were included as predictors. Tests of moderation were conducted by examining regression coefficients of interaction terms for module and time. Correlation in client outcomes due to common GCBT participation was modeled using random session effects. To mitigate potential bias and variance inflation, we restricted the random session effects' contributions to be orthogonal to those of the session-level moderators.
Results: The restricted models had better model fit statistics. Module did not significantly moderate the reduction in depressive symptoms for residential GCBT clients. The People module was associated with significantly greater decreases in symptoms than the Thoughts module in the outpatient sample (95% CI:(-.75,-.03)).
Conclusions: Our approach results in improved model fit and more precise tests of moderation. Our findings about module theme as a moderator of change in depressive symptoms are mixed. This is a secondary data analysis, which limits the generalizability of our results relative to a study primarily designed to test for module effects, yet our findings support further research into this topic and demonstrate the importance of our analytic approach to exploring the effect of session-level characteristics on outcomes.
Financial Support: NIH/NIAAA Grant R01AA019663

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BARRIERS PREVENTING PRIMARY CARE PATIENTS FROM REDUCING DRUG USE.

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Aims: Primary care providers can deliver brief intervention services to reduce the frequency and intensity of patients' drug use. To improve the efficacy of brief interventions, providers need knowledge of the barriers that patients believe inhibit them from changing their drug use behaviors. The aim of this paper is to identify the major barriers that primary care patients believe inhibit drug use behavior change, and determine if any barriers are associated with the use of any specific classes of drugs.
Methods: Qualitative data from telephone health education sessions with 103 recipients of a primary care-based brief intervention to reduce drug use were analyzed using grounded theory coding strategies to identify barriers participants believed prevented them from changing drug use behaviors. The authors examined the prevalence of barriers and how barriers varied among users of different classes of drugs.
Results: The most common barriers to drug use behavior change were needing drugs to alleviate mental/emotional distress, proximity to people/places associated with drug use, belief that drug
use enhanced quality of life/functioning, needing drugs to alleviate physical pain/discomfort, fear of abstaining, and challenges associated with poverty/homelessness. High proportions of marijuana
and prescription pain medication users cited reliance on drugs to alleviate physical discomfort, high proportions of marijuana and cocaine/crack users cited belief that drug use enhanced their quality
of life/functioning, and high proportions of crack/cocaine and amphetamine users cited proximity to people/places associated with drug use and poverty/ homelessness as barriers to drug use behavior change.
Conclusions: A variety of health-related and socio-economic challenges inhibit at-risk drug users from changing their drug use behaviors. Brief interventions should target not only drug use behaviors themselves, but also the barriers that patients cite as obstacles to drug use behavior change.
Financial Support: NIDA Grant R01DA022445, NIDA Grant T32DA07272-20, NCRR/NCATS UCLA CTSI Grant UL1TR000124

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NICOTINE RESEARCH CIGARETTES FOR THE NIDA DRUG SUPPLY PROGRAM.

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Aims: To characterize and supply nicotine research cigarettes on behalf of the NIDA drug supply program for distribution to research investigators.
Methods: Nicotine Research Cigarettes (NRCs) have been manufactured under the Spectrum brand for the National Institute on Drug Abuse (NIDA) for use in research programs. Nine million cigarettes were manufactured in 24 batches with nicotine delivery levels ranging from <0.05 to >1.5 mg/cigarette. Regular and menthol cigarettes were produced with each of 8 different blends of varying nicotine content and design features, including filters and ventilation. All 24 batches were characterized for nicotine, menthol and minor alkaloid content and yield; moisture content and yield; CO yield; tar yield; and TPM. The cigarettes were stored in freezers at -25 to -10 oC. For stability study purposes, samples of all batches were stored at room, refrigerator, and freezer temperatures. These samples will be monitored periodically for alkaloid and moisture content. The cigarettes are distributed according to the NIDA drug supply guidelines.
Conclusions: All batches of Nicotine Research Cigarettes are now available for research with NIDA approval through the NIDA drug supply program and are being monitored for stability.
Financial Support: This work was funded by NIDA.

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COCAINE-SEEKING IS DOSE DEPENDENTLY ENHANCED BY HIV-1 TAT PROTEIN EXPRESSION IN MALE AND FEMALE MICE.

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Aims: Substance abuse is comorbid with HIV infection. The HIV-1 viral accessory protein, Tat, has demonstrated neurotoxic effects that occur synergistically with drugs of abuse and may be ameliorated in the presence of sex steroids such as estradiol and/or progesterone. Among people and rodent models, cocaine seeking is greater among males compared to females, and is influenced by sex steroid variations. The present investigation aimed to assess (1) whether central expression of HIV-1-Tat could influence cocaine seeking in a whole-animal mouse model, as well as (2) whether endogenous cyclical changes in sex steroids can ameliorate acute effects of Tat on cocaine-seeking behavior.
Methods: Experiments used GT-tg bigenic mice (n=15-20/group), which express Tat protein under doxycycline (Dox) treatment. One week following Dox (0, 25, 50, or 125 mg/kg, i.p.) treatment, proestrous or diestrous female mice were paired with male counterparts and underwent cocaine (10 mg/kg/d, s.c.) conditioned place preference (CPP) with assessments occurring on days of proestrus (high-hormone status) or diestrus (low-hormone status).
Results: Data recapitulated effects observed in clinical populations. Male GT-tg bigenic mice demonstrated a significantly greater cocaine-CPP compared to the response of female GT-tg mice. Among males, induction of Tat protein dose-dependently potentiated cocaine-CPP. However, these effects were influenced by hormone status among females. Female mice on proestrus (high-hormone) had a significantly attenuated potentiation of cocaine-CPP compared to those on diestrus.
Conclusions: HIV-1-associated Tat protein may mediate drug-seeking sequelae that are associated with viral infection. Fluctuations in endogenous hormones may modulate HIV-related pathology, underlying the sex differences observed in behavioral dysfunction.
Financial Support: Funding was provided by NIMH (MH085607 to JPM) and the State of Florida, Executive Office of the Governor's Office of Tourism, Trade, and Economic Development.

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COMPARING THE PREVALENCE OF CONCURRENT BENZODIAZEPINE PRESCRIPTION AMONG VETERANS RECEIVING METHADONE VS. BUPRENORPHINE MAINTENANCE THERAPIES.

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Aims: Benzodiazepine (BZD) use in the context of opioid agonist therapy (OAT) has been associated with an increased risk of adverse outcomes. Our objective was to measure the recent prevalence of concurrent BZD prescription among patients receiving OAT in the Veterans Health Administration (VHA) by OAT type (methadone vs. buprenorphine).
Methods: This was a retrospective cohort study of all VHA patients receiving methadone or buprenorphine between fiscal years (FY) 2006-2010 using administrative data. Because methadone is not recorded in pharmacy records, methadone patients were identified by presence of at least two visits to a VHA OAT clinic in a single FY and the absence of a buprenorphine prescription. Buprenorphine patients were identified by the presence of a buprenorphine prescription. BZD exposure was determined using dates of fill and days supply. Concurrent BZD and OAT exposure was determined by measuring overlap between BZD fills and OAT treatment. Group-level analysis was performed using a Poisson regression model.
Results: We identified 11,075 unique methadone and 8,600 unique buprenorphine patients during FY06-10. A greater proportion of buprenorphine patients (24.3%) received at least one concurrent BZD than methadone patients (19.71%; $p < 0.001$). When the proportion of patients receiving concurrent BZDs in FY06 was compared to patients in FY10, no difference was found within the methadone (14.22% vs. 13.87%; p=0.17) or buprenorphine groups (18.09% vs. 20.05%; p=0.61).
Conclusions: Despite the potential risks associated with concurrent BZD and OAT use, more than a fifth of all patients receiving OAT have also received a concurrent BZD prescription in recent years. That concurrent BZD prescription is more common in buprenorphine than in methadone may reflect differences in the relative perceived safety of these opioids. Further work is needed to measure the impact this practice might have on the risk of adverse outcomes.
Financial Support: Grant no. IIR-08-071 from HSR&D of the Department of Veterans Affairs.

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RECENTLY ABSTINENT METHAMPHETAMINE USERS SHOW INCREASED RECRUITMENT OF PREFRONTAL CORTEX DURING VALUATION: AN FMRI STUDY.

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Aims: Aims: Valuation is an important process for decision-making and other daily activities. One approach to examine this process is to use the willingness-to-pay task (WTP). During this task, subjects bid on a series of visually presented food items on a scale ranging from 3 to -3 dollars where positive and negative bids represent how much the subjects is willing to pay for the opportunity to eat appetitive food items or to avoid eating aversive food items respectively. In this study, we examined whether neural processing during the WTP task differs between recently abstinent methamphetamine users (MU) and healthy controls.
Methods: Methods: 17 MU and 18 age matched controls participated in the study. MU were enrolled in an inpatient drug treatment program and had been sober for 36 days on average. Quantity of drug use, recency, age of onset and psychiatric history were assessed during a clinical interview. Controls subjects did not report any current or past substance use dependence. fMRI data were acquired with a 3T GE scanner.
Results: Results: In both groups, activity that scaled monotonically with the value of bids was observed in a network of regions consistent with prior research, namely the vmPFC, pCC, precuneus, and striatum. A t-test comparing the two groups, found two clusters of significantly greater activity in MU: the right dlPFC and the right anterior temporal cortex (aTC). Activity in the right aTC correlated positively with age at onset of methamphetamine use ($r = 0.59$, $p < 0.05$).
Conclusions: Conclusions: While MU and controls recruit the same network of brain regions during WTP, MU exhibit significantly greater activation in the dlPFC and superior temporal gyrus. Neural activity in the dlPFC has been linked to attentional modulation of the WTP signal in previous studies. Thus, MU may require additional attentional resources when evaluating food items, pointing toward a basic inefficiency in these individuals that could contribute to difficulty in making appropriate choices.
Financial Support: Financial Support: NIDA 5P20DA027843

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DISSEMINATING PREVENTION THROUGH CULTURAL ADAPTATION RESEARCH WITH LATINO POPULATIONS.

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Aims: To compare and contrast the levels of cultural acceptability and feasibility in two differentially culturally adapted parenting interventions being disseminated among low-income Latino immigrants
Methods: This NIMH-funded RCT study was developed to compare and contrast two differentially culturally adapted versions of the evidence-based intervention known as Parent management Training-the Oregon Model. Participants were randomized into one of three conditions: (a) CAPAS-Original, (b) CAPAS-Enhanced, or (c) a wait-list control group. Measurements of parent-child interactions, parenting skills, and child internalizing and externalizing behaviors are being taken at baseline, intervention completion, and 6-month follow-up. A total of 87families have participated in the study.
Results: The RCT phase of this investigation is just being completed and collection of outcome data will be completed by Fall 2013. Preliminary RCT phase of the study will be presented consisting of initial quantitative and qualitative satisfaction indicators. Preliminary findings indicate high participant satisfaction with both culturally adapted versions of the intervention. No statistical differences were found between CAPAS-Original and CAPAS-Enhanced on any of the weekly session satisfaction ratings. According to qualitative data, however, participants in both interventions considered critical to increase the number of culturally-focused sessions on immigration and biculturalism.
Conclusions: Current findings indicate that the value of cultural adaptation research lies in its potential to identify which elements of an original intervention as well as which culturally adapted components are considered by target populations to be most relevant.
Financial Support: This investigation was supported by Award Number R34MH087678 from the National Institute of Mental Health.

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SUBSTANCE USE IN ADOLESCENTS WITH ENVIRONMENTAL LEAD EXPOSURE IN CHILDHOOD.

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Aims: Lead has long been established as a potent neurotoxin, damaging the developing nervous system in children and potentially interfering with their long-term behavioral development.Cross-sectional studies have reported an association between early lead exposure and behavior problems as well as psychiatric comorbidity in later childhood and adolescence, but little is known about environmental lead exposure in childhood and later drug abuse. In 2001 a small cohort of children were identified with elevated blood lead levels(BLL) in Montevideo, Uruguay.
The present study investigated whether 2001 BLL or current BLL (2011) collected had an effect on drug use in this group of adolescents.
Methods: Children with elevated BLL's in 2001 were re-identified and tested for current BLL using atomic absorption spectrometry in 2011. A total of 89 adolescents who agreed to participate in the study completed an assessment focused on social and demographic variables including educational status, grade in school, health comorbidities, and patterns of substance use. The CRAFFT screening tool was administered to the adolescents in 2011. To examine the influence of lead levels in childhood and adolescence on substance use as measured by the CRAFFT logistic regression analyses were conducted.
Results: Over 90% of the sample had BLL above 10 ug/dl in 2001 (mean BLL in 2001 were 14.2 ug/dl). During adolescence (mean age 14.6, 57% male) mean BLL were 5.04 ug/dl. About 5% of the adolescents reported smoking, 41.6% reported using alcohol, 9% used marijuana and 5% of the sample received a score of 2 or higher on the CRAFFT. Logistic regression analyses revealed that lead levels in 2011 increased the odds of adolescents using tobacco by 2.27, controlling for the effect of covariates and lead levels in 2001.
Conclusions: In addition to the previously known effects of lead on development, the results of this study suggest that exposure to lead in childhood acts as a risk factor to tobacco use in adolescence.
Financial Support: No financial support

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INFLUENCE OF BUPROPION ON SMOKING ABSTINENCE IN OPIOID-MAINTAINED SMOKERS.

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Aims: Rates of smoking among opioid-maintained patients are 3-fold that of the general population and smoking cessation interventions in this population have shown modest outcomes. We have developed an efficacious behavioral intervention to promote smoking abstinence among methadone- and buprenorphine-maintained smokers. While not a primary focus, we offer bupropion (Zyban) as an optional pharmacotherapy for interested and eligible patients. In the present analyses, we evaluated the contribution of bupropion to smoking abstinence, retention and nicotine withdrawal among smokers receiving financial incentives contingent on abstinence.
Methods: All participants received a 2-week intervention that included daily visits, biochemical verification of smoking status and reinforcement of abstinence.
Results: Participants (35 Bupropion (B), 49 No Bupropion (NB)) were 41% male, 33 yrs, and reported smoking 18.6 cigarettes/day. Overall levels of smoking abstinence were generally high, with participants providing 54% abstinent samples during the study. Smoking outcomes did not differ between B and NB groups, with 60% and 51% abstinent samples provided during the study, respectively (p=.23). There was a trend toward longer treatment retention in the B vs. NB group, with 80% and 61% of participants retained at the end of study, respectively (p=.07). No significant differences were seen between groups on severity or timecourse of nicotine withdrawal (p>.05).
Conclusions: There was no significant contribution of bupropion on smoking-related outcomes in the present study, though our ability to evaluate this could be limited by the potency of the behavioral intervention itself. These data are consistent with prior studies showing modest effects of smoking pharmacotherapies in this population, perhaps due to the complex interactions between nicotine and the endogenous opioid system. However, the efficacy of our behavioral intervention suggests that this challenging population of smokers is sensitive to reinforcement-based interventions.
Financial Support: R01 DA019550, T32 DA007242

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TRANSACTIONAL SEX AMONG AN EMERGENCY DEPARTMENT SAMPLE: EXPLORING GENDER, SUBSTANCE ABUSE AND HIV RISK.

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Aims: Men and women involved in transactional sex (TS) report increased rates of HIV risk behaviors and substance abuse problems as compared to the general population. When people engaged in TS seek healthcare, they may be more likely to utilize the emergency department (ED) rather than primary care services. Our goal was to examine the prevalence and correlates of TS involvement among an emergency department (ED) sample of men and women.
Methods: Adults ages 18-60 were recruited from an urban ED, as part of a larger randomized control trial. Participants (n=3,699; 2,428 women, 1271 men) self-administered a screening survey that assessed both substance use and HIV risk behaviors, including transactional sex (i.e. being paid for the exchange of a sexual behavior for money, drugs, or other needs).
Results: Of the sample, 13.6% reported TS involvement within the past three months (62% were female). Bivariate analysis showed TS involvement was positively associated with alcohol use (OR=1.02), drug use (OR=1.83) and HIV risk behaviors, including inconsistent condom use (OR=5.63) and multiple partners (OR=1.37). These variables remained significantly positively associated in a multivariate regression analysis. Gender findings were non-significant.
Conclusions: The prevalence rates of both men and women in the ED who report recent TS involvement are substantial. These individuals were more likely to report higher rates of alcohol/drug use and other risky sexual behaviors. As such, the ED may be a prime target location to engage both men and women who are involved in TS into substance use interventions.
Financial Support: This investigation was supported by the National Institutes of Health under Ruth L. Kirschstein National Research Service Award T32 DA007267 and NIDA #026029. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

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CHARACTERIZATION OF PLACENTAL EFFLUX TRANSPORTERS.

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Aims: P-glycoprotein (P-gp), Breast Cancer Resistance Protein (BCRP), and several Multidrug Resistance Proteins (MRP's) are expressed in the human placenta. The major function of placental efflux transporters is to decrease fetal exposure to xenobiotics including medications used for treatment of the pregnant patients e.g. opiates and bupropion. The aim of this investigation is to characterize the activity of P-gp and BCRP using their respective prototypic substrates [3H]-Paclitaxel, Taxol & [3H]-Estrone-3-Sulfate, E1S.
Methods: Inside-out brush-border membrane vesicles (IOV) were prepared from term placentas (n=10). ATP dependent uptake of E1S and Taxol by IOV was calculated as the difference in uptake of each substrate in the presence and absence of ATP. The chemical inhibitors to P-gp (verapamil, haloperidol), BCRP (Ko143, fumitremorgin C), and MRPs (indomethacin, pravastatin, bromosulfalein) were used to identify the efflux transporters contributing to placental vesicular uptake of E1S and Taxol.
Results: Results: The kinetic parameters determined for ATP dependent uptake of E1S and Taxol by IOV revealed the following apparent Kt values; 670 ± 200 nM and 66 ± 38 nM and Vmax values of 0.8 ± 0.2 pmol * mg protein-1 * min-1 and 4.5 ± 0.5 pmol * mg protein-1 * min-1, respectively. The ATP-dependent uptake of Taxol was significantly reduced in the presence of P-gp (50-70%) and MRPs (60-70%) inhibitors while ATP-dependent uptake of E1S was 40-60% reduced by MRPs and 20% by BCRP inhibitors.
Conclusions: Previously Taxol and E1S were characterized as prototypic substrates of P-gp and BCRP using P-gp and BCRP vesicles prepared from recombinant baculovirus-infected insect cells. The data obtained in this investigation revealed that ATP-dependent uptake of these substrates by placental IOV are mediated by more than one transporter. These data suggest that most likely multiple transporters are involved in the in vivo efflux of different substrates/medications.
Financial Support: NIDA R01DA13431 (MSA), NIDA R01DA030998 (TN), NICHD T32HD55163

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IS PRIMARY CARE ACCESSIBLE TO GENERAL POPULATION ADULTS WHO USE DRUGS?

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Aims: Illicit drug use is common in adults; however, data regarding the impact of drug use on health service utilization is scarce outside of clinical addiction populations. The Coronary Artery Risk Development in Young Adults study (CARDIA) was used to study whether the longitudinal trajectories of both marijuana and non-marijuana drug use were associated with reduced primary care (PC) access at 18-year follow-up.
Methods: A cohort of 4300 healthy young adults was repeatedly queried about drug use from 1987-88 to 2005-06. We compared self-report of having a usual PC provider at end follow-up (ages 38-50) among trajectories (using SAS PROC TRAJ) for non-marijuana drug use (cocaine, opioids, amphetamines) and marijuana use. Models were adjusted for demographics, insurance, health status, tobacco & alcohol.
Results: For non-marijuana drugs, there were 160 (3.7%) Persistent Occasional users, 110 (2.6%) Early Frequent/ Late Occasional users, 340 (7.9%) Early Occasional users and 3690 (86%) non-users. Persons with continuing drug use were more likely to lack PC at follow-up (42%, 26%, 20%, 15% for the 4 groups, respectively, p<.001). Adjusting for covariates, the association was significant for Persistent Occasional Users only (OR 1.7, 95%CI 1.1-2.8). Differences for marijuana trajectories were similar, but less pronounced (30%, 25%, 24%, 20% and 13% for Persistent, Decreasing, Increasing, Occasional and Non-users, respectively, p<.001). The lack of PC was more common for the Increasing marijuana trajectory group (OR 1.7, 95% CI 1.0-2.7) after adjustment.
Conclusions: Among adults in the general population, 4 in 10 persistent non-marijuana drug users and 3 in 10 marijuana users lacked primary care in middle age. The unsettled question of whether to screen for drug use in primary care should include consideration of who might be missed.
Financial Support: NIDA R01-DA-025067; NHLBI N01-HC-95095; N01-HC-48047

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BRIEF ONLINE INTERVENTIONS TARGETING RISK AND PROTECTIVE FACTORS FOR INCREASED AND PROBLEMATIC ALCOHOL USE AMONG AMERICAN COLLEGE STUDENTS STUDYING ABROAD.

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Aims: Research documents increased and problematic alcohol use during American student study abroad experiences. Despite increasing numbers of students studying abroad each year and a growing concern about this high-risk event, there is no research available documenting efficacious preventive programs for these students. Previous work suggests perceptions of study abroad peer drinking and host country native adult drinking are risk factors for increased alcohol use while abroad, while components related to positive Sojourner Adjustment (i.e., healthy temporary cultural adjustment) may protect against problematic use.
Methods: Employing a 2 x 2 longitudinal randomized controlled intervention design, the present study sought to prevent increased and problematic alcohol use by correcting misperceptions of peer norms and by promoting positive and healthy adjustment into the host culture through brief online personalized feedback interventions. A sample of 343 study abroad students were randomly assigned to one of four conditions including a personalized normative feedback intervention (PNF), a Sojourner Adjustment feedback intervention (SAF), a combined PNF + SAF intervention, and an assessment only control condition.
Results: Multilevel regression analyses revealed that, contrary to hypotheses, participants in the SAF intervention condition increased their drinking by a rate of 31% during the first month abroad compared to control. In contrast, SAF and PNF participants reported a 31% and 27% reduction, respectively, in alcohol-related consequences compared to control participants during the last month abroad.
Conclusions: This research represents an important first step in designing and implementing efficacious interventions with at-risk study abroad college students using online methodologies with normative information and Sojourner Adjustment content.
Financial Support: 1F31AA018591 awarded to Eric Pedersen from NIAAA

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TRAJECTORY OF TREATMENT, HOSPITALIZATION AND RELAPSE OF CRACK USERS.

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Aims: This study mapped the treatment trajectories of male crack users describing the attempts for hospitalization and relapse after discharge.
Methods: Cross-sectional study with 207 male inpatient crack users. We used a form with demographic data and the Questionnaire for Treatment Trajectories of Crack Users.
Results: In the search for hospitalization, 50% have tried up to 2 times (Mean = 2.12 times) to succeed. Between the first attempt and hospitalization, 50% of the sample waited up to 3 days (mean = 6.47 days), with 92.8% of the sample admitted in public health. Crack users of this study indicated that the main factors influencing relapse after discharge from the first admission were occupational problems (65.5%) and legal problems (62.1%). In their own perception, the main factors that can influence abstinence after discharge were medication (92.3%) and ability to handle risky situations (96.6%). Of the total sample, 144 patients (69.6%) reported previous hospitalizations on an average of 2.26 times, totalizing 357 inpatient admissions. The average length of stay was 52.83 days (median = 28 [16.25; 36.75]). Out of 357 admissions, about 322 (90%) showed relapse after discharge, and half of these relapses occurred in less than 30 days (median = 30 [6, 120]), an average of 90 days between discharge from hospital and relapse using crack.
Conclusions: In this study, the majority of the subjects had relapse to the use of crack less than a month after discharge, indicating the need to develop inpatient treatments suitable to prepare the crack user for abstinence in front of factors that influence relapse.
Financial Support: Brazilian Secretariat for Drug Policies (SENAD), project number # 10/0002

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WHAT HAPPENS WHEN STABILIZED METHADONE-MAINTAINED DOSE MUST BE CHANGED ?

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Aims: Adequate methadone dose is highly important to patients' success in Methadone Maintenance Treatment (MMT). Stable dose was found to be related to multiple factors including environmental and genetics. The individual stable methadone dose is determined by patients' report, clinically, and laboratory results. However, through treatment, various medical reasons may lead to change the stabled methadone dose (i.e. prolonged QTc, non therapeutic level of blood methadone, etc). Our aims to follow up stabilized patients following dose change, and to evaluate whether patients can be stabilized on different methadone doses during their treatment.
Methods: Inclusions were 138 patients who were clinically stabilized (steady methadone dose and no opiate, cocaine, amphetamine for at least 3 months) and their methadone blood level was checked before first take-home dose (Group 1, n=93), or annually (Group 2, n=45)). Group 3 were 20 stabilized patients whose dose was reduced due to QTc prolongation.
Results: Of the 158 patients who were stabilized when evaluated for methadone level or QTc (methadone dose 138.6±46.1mg/d), dose change was needed in 86 patients (a decrease in 75 (20.4%, 80% and 100% from groups 1, 2 and 3 respectively) and an increase in 11 from group 1). Specifically, among 56 patients the dose was reduced less than 15% of their maintained dose, and among 19, 15% or above. Stabilization with the new dose was achieved among 74.4% of the 86 patients (73.3% of the reduced- and 81.8% of the elevated-dose) similar to 80.6% of 72 patients who did not have to change dose and stabilization evaluated for additional 3 consecutive months.
Conclusions: The change of adequate stable dose for therapeutic and safety reasons is at times essential. A new stabilization is achieved in most patients (74%) as compared in those with no dose change. Future study is needed to study whether these patients, who achieved stabilization despite the dose change, are those who may never need the higher dose, or that the stabilization dose may change over time.
Financial Support: Adelson Family Foundation

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SUBGROUP DIFFERENCES IN TRAJECTORIES OF HEROIN USE AND TREATMENT EFFECTIVENESS: AN INTERSECTIONALITY VIEWPOINT.

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Aims: Previous studies have shown differences in substance use and treatment efficacy among racial groups and between men and women. However, the role of age is often neglected, and few studies have examined how gender and race intersect to affect individual substance use problems and their recovery after treatment. The aim of this study is to examine how trajectories of heroin use after admission to treatment are jointly affected by age, gender, and race, using an intersectionality approach.
Methods: Data come from the longitudinal Drug Abuse Treatment Outcome Studies, including a total of 10,010 patients in long-term residential, outpatient drug free, outpatient methadone, or short-term inpatient treatment at intake; 2966 patients remained at 1-year follow up and 1393 patients at 5-year follow-up. We utilized four items measuring heroin use to comprise a severity scale of heroin use. All items were repeatedly measured. Scores for each individual at each time point were computed. Socio-demographics were measured at baseline (age:<=32 vs. >32; gender: male vs. female; race: White vs. African American vs. Hispanic). We use growth curve modeling to explore the change of heroin use and treatment effectiveness of different modality among twelve age/gender/race demographic groups.
Results: Both the initial level and change in severity of heroin use vary significantly by modality and by demographic groups. In all, patients in methadone treatment had higher severity of heroin use both at intake and across time compared to patients in other treatment modalities. Compared to younger White males, both elder African American females and males, younger Hispanic females, and both elder White females and males had significantly lower severity scores across time. In addition, a model also suggested a moderating effect of the demographic groups on the treatment effect of different modality.
Conclusions: The findings highlight the utility of an intersectionality approach to understand the differences in drug use problems and trajectories of recovery after receiving treatment.
Financial Support: Financial Support: Supported by NIDA R21 DA025252, P30DA016383, & K05DA017648 (PI: Hser)

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SMART RECOVERY®: AN EFFECTIVE GROUP METHOD FOR CO-OCCURRING CONDITIONS IN COMMUNITY TREATMENT.

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Aims: This presentation will demonstrate, from our research and practice, that SMART Recovery® is useful for group treatment of co-occurring conditions (CC).
Methods: SMART Recovery® (SMART) is a group self-help modality based upon REBT (www.smartrecovery.org). We conducted several studies using SMART: 1. A multi-year study comparing SMART with 12-Step based IOP treatment for CC (assessments = ASI, etc). 2. Focus groups were formally analyzed with persons with CC: treatment experiences and recommendations from men, women and LGBTQ persons, experiences seeking treatment for physical health problems, and groups conducted with clients and counselors who had used both 12-Step and SMART methods. 3. A SMART & Healthy group was created to promote health behavior change for persons with CC. (BASIS-32, SF-12).
Results: 1. Our IOP SMART program for CC significantly reduced alcohol use and increased employment and health status on the ASI through 12-month follow-up (Penn & Brooks, 1999; Brooks & Penn, 2003). Qualitative data indicated that clients preferred the SMART program. 2. The focus groups demonstrated that the SMART methods fit the qualities that clients desire for treatment of CC. Clients and counselors like SMART, find it easy to learn and use, use the skills in diverse situations, find it effective for participants at several stages of change, and it's client-centered (Penn, Brooke, Brooks, & Gallagher, 2004). 3. SMART & Healthy was well received and results indicated significant improvement in overall BASIS-32 scores, SF-12 physical functioning & social functioning, less emotion-focused coping, and improved working alliance (Gallagher, Brooks, & Penn, 2006).
Conclusions: We found SMART to be an effective, versatile group method for co-occurring conditions in community behavioral health treatment settings. It is useful for many types of co-occurring conditions, user friendly, easily trained, feasible, client-centered and cost-effective.
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CHANGES IN SUBSTANCE USE AND SEXUAL RISK OVER TIME AMONG BLACK MSM AND BLACK MSMW IN 6 U.S. CITIES.

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Aims: To identify differential reductions in rates of reported substance use and self-reports of high risk sexual behavior over a one year time period comparing Black men who have sex with men (BMSM) and Black men who have sex with men and women (BMSMW) in 6 US cities.
Methods: The present study utilized baseline, 6 month and 12 month follow-up data from the HIV Prevention Trials Network Brothers Study (HPTN 061), a feasibility study of a multi-component intervention for Black MSM in 6 US cities. We assessed change over time in psychosocial factors, substance use, and sexual risk behaviors and compared the change in MSMW with that in MSM using generalized estimating equation (GEE) models. Outcomes included self-reported crack cocaine use, methamphetamine use, internalized homophobia (IHP), and alcohol use within 2 hours of last anal intercourse. Each GEE model included sexual behavior category, duration in the study (in years) and their interaction as covariates.
Results: Compared with MSM, MSMW reported higher use of crack cocaine (OR: 1.8, 95% CI: 1.4-2.3), higher IHP (OR: 1.7, 95% CI: 1.4-2.0), but similar use of methamphetamine (OR: 1.0, 95% CI: 0.7-1.4). Crack cocaine and methamphetamine use as well as IHP declined after enrollment at a similar rate for both groups. There was a significant interaction of sex behavioral category and time for alcohol use during unprotected anal sex at last intercourse. At baseline, more MSMW reported using alcohol during unprotected anal sex compared to MSM (OR: 1.5, 95% CI: 1.2-1.9). MSMW had a bigger decrease in alcohol use during UAI (OR: 68%, 95% CI: 58-76%), compared with MSM (OR: 54% 95% CI: 42-63%) during the one year follow-up period.
Conclusions: Alcohol use is an important factor to be considered in developing risk reduction interventions for Black MSMW.
Financial Support: This study was supported by NIAID, NIDA, and NIMH under cooperative agreement #UM1 AI068619 as part of the HPTN Scholars Program, UCLA HATT Program (R25 MH-080644) and Project DISRUPT (R01 DA-028766)

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ALCOHOL AS A PREDICTOR OF VIOLENCE VICTIMIZATION AMONG U.S. COLLEGE STUDENTS: AN ANALYSIS OF SEX DIFFERENCES.

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Aims: We test whether violence victimization is predictive of heavy episodic drinking (HED) and test for sex differences. Males and females with histories of victimization were hypothesized to be more likely to engage in HED than those not victimized.
Methods: We collected survey data from undergraduates at a Midwest university (N=353). Two domains of victimization were considered: intimate partner violence (IPV) and non-intimate victimization. Types of violence included physical, sexual, and verbal victimization. In logistic regression models, HED was regressed on each type and domain of victimization. Control variables included race and employment status. We tested for interactions between sex and victimization. To test for sex as a moderator, we created crossproduct terms between victimization type and sex.
Results: Forty-six percent engaged in HED; 36% reported victimization. Physical IPV increased the odds of HED (OR=6.01, p<.05). Experiencing a combination of IPV types increased the odds of HED (OR=2.02, p<.05). Being female marginally decreased the odds of HED for any violence history (OR=.650, p<.10). Models that contain the interaction terms for victimization by sex reveal the main effect for experiencing multiple types of IPV was marginally significant (b= -1.04, OR=.353, p<.10) as was the interaction term (b=2.06, OR=7.88, p<.10). Females experiencing physical IPV (OR=.839, p<.05) or experiencing a combination of IPV types (OR=4.45, p<.01) increased the odds of HED. Females who experience sexual victimization had marginally significant increased odds of HED (OR=3.68, p<.10); males who experienced any interpersonal victimization had increased odds of HED (OR=8.92, p<.05).
Conclusions: Partial support for the link between violence and HED by sex were found. Pilot findings suggest men and women have different victimization experiences and exhibit different behavioral drinking patterns in relation to victimization history. Violence victims may be at risk for developing problematic drinking behavior. The implementation of HED treatment efforts should consider victimization histories.
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THE EFFECT OF VIRTUAL CUE EXPOSURE THERAPY ON BACKGROUND AND CUE EXPOSURE CRAVING.

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Aims: Two types of craving have been identified: cue exposure and background. Cue exposure craving is an episodic desire that increases quickly after the exposure to smoking-related cues. Background craving is a tonic state that gradually decreases during days after quitting. Few laboratory studies have examined the effect of cue exposure therapy (CET) on craving over sessions. Results have shown that cue induced craving is difficult to attenuate. Background craving can be reduced with nicotine replacement therapy, but no effect has been reported with CET. The aim of this study was to assess the effect of CET through virtual reality on cue induced and background craving.
Methods: Smokers (n=42) received 5 sessions of CET through Virtual Reality. Inclusion criteria were: smoking at least 10 cigarettes per day, being able to wear a virtual reality eyewear and meeting the DSM-IV diagnosis of nicotine dependence. Craving was assessed through a visual analogue scale from 0 to 100. Background was assessed before the start of each exposure. Cue exposure was evaluated during the virtual exposure.
Results: Repeated measures ANOVA showed that levels of background craving ($F(4, 164) = 12.96$, $p < .001$) and cue induced craving ($F(4, 164) = 25.38$, $p < .001$) changed significantly during treatment. Post hoc comparisons showed a significant reduction on background craving and cue induced craving after treatment compared to the levels on both types of craving in the first treatment session.
Conclusions: Virtual cue exposure therapy reduced both types of craving: background and cue-induced. Contrary to previous studies, our results showed an effect of CET over sessions on background and cue exposure craving. Also, this study showed that VR provides an alternative for cue exposure therapy over traditional methods to treat background and cue exposure craving.
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SEX MODULATES APPROACH SYSTEMS AND IMPULSIVITY IN SUBSTANCE DEPENDENCE.

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Aims: Personality traits such as pathological engagement in approach behaviors, high levels of impulsivity and heightened negative affect are consistently observed in substance dependent individuals (SDI). The clinical course of addiction has been shown to differ in women compared to men. For example, women increase their rates of consumption of some drugs of abuse more quickly than men. Despite the potential influence of personality traits and sex in the development of addiction, few studies have investigated the interaction of these factors in substance dependence.
Methods: 51 SDI (26 male, 25 female) and 66 controls (41 male, 25 female) completed the Behavioral Inhibition/Behavioral Activation (BIS/BAS) Scales, the Barratt Impulsiveness Scale, and the Positive and Negative Affect Schedule (PANAS-X). Data were analyzed using a 2x2 ANCOVA testing for main effects of group and sex and group x sex interactions, while adjusting for education which differed across group.
Results: Significant group x sex interactions were observed for BAS scores [$F(1,116)=7.03$, $p<.01$] and Barratt Motor Impulsiveness [$F(1,116)=6.11$, $p<.02$] with female SDI showing the highest approach tendencies and impulsivity, followed by male SDI, male controls, and finally female controls. Main effects of group were found for BAS [$F(1, 116)=27.54$, $p<.00$], Barratt Impulsiveness [$F(1, 116)=23.45$, $p<.00$], and negative affect [$F(1, 116)=25.23$, $p<.00$] with SDI scoring higher than controls on all 3 measures. Behavioral Inhibition System scores were higher in women than men [$F(1,116)=14.03$, $p< 00$].
Conclusions: Higher BAS and motor impulsivity in SDI women relative to SDI men or control women suggests that personality traits associated with drug use may be modulated by sex. These factors may contribute to differences in the disease course observed in male compared to female drug users.
Financial Support: Funding for this study was provided by NIDA grants R01 DA024104 and DA027748.

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RATS THAT SELF-ADMINISTER METHAMPHETAMINE SHOW PARKINSON'S DISEASE-LIKE INFLAMMATION AND α-SYNUCLEIN NEUROPATHOLOGY.

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Aims: Abuse of methamphetamine (meth), a potent psychostimulant, appears to increase the risk for developing Parkinson's disease (PD) (Callaghan et al. *Drug Alcohol Depend* 120,2012). This enhanced vulnerability may relate to the known neurotoxic effects of meth *via* oxidative stress, mitochondrial dysfunction and inflammation (Yamamoto et al. *Ann NY Acad Sci* 1187,2010), factors also implicated in PD pathology. However, *in vivo* studies assessing meth-induced toxicity are largely based on acute, high doses of non-contingently administered meth. It is unknown if similar outcomes occur with meth administration protocols that better emulate human drug-taking, e.g., self-administration. The current study determined if meth self-administering rats exhibited markers of inflammation, i.e., glial fibrillary acidic protein (GFAP; marker of glial cell activation) and tumor necrosis factor-α (TNF-α; pro-inflammatory cytokine). To substantiate the concept that meth abuse enhances vulnerability for PD, we assayed the SN for α-synuclein, a neuropathological hallmark for PD.
Methods: Male Sprague-Dawley rats self-administered meth for 14 days; rats were sacrificed and tissue harvested on day 15. Saline-yoked rats served as controls. Western blotting was used for harvested rostral striatum (rSTR) and substantia nigra (SN), the terminal and cell body regions (respectively) of dopamine neurons most severely affected in PD.
Results: Meth self-administration increased GFAP and TNF-α levels in the rSTR and SN ($p<0.01$). In the SN, α-synuclein was also increased in METH-treated rats compared to saline controls ($p<0.0001$).
Conclusions: These brain changes occur in the absence of any detectable degradation in motor function. These results provide the first evidence for PD-like pathology in meth self-administering rats, and therefore offer insight into mechanisms underlying the enhanced vulnerability of meth abusers to develop PD.
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IMPACT OF RACE AND AGE ON TREATMENT COMPLETION AMONG ADULT MARIJUANA USERS.

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Aims: The prevalence of marijuana use disorders has increased significantly among African American (A-A) adults in recent years. A-A young adults (aged 18-25) are less likely to complete marijuana treatment than their White counterparts, but it is not clear if these trends extend beyond the young adult years.
Methods: This study examines 2 samples of adults receiving community-based outpatient substance abuse treatment and reporting primary marijuana use. Sample #1 (N = 160) was composed of adults in the southeastern US, 70.6% of whom were A-A, with a mean age of 27.9 years. Sample #2 (N = 324) was composed of adults in the US mid-Atlantic region, 38.3% of whom were A-A, with a mean age of 25.0 years. In both samples, treatment completion was defined as regular treatment attendance, sustained negative urine drug screens, participation in 12-step groups, and achievement of individualized treatment goals.
Results: In Sample #1, treatment completion was significantly associated with the interaction of race and age (odds ratio [OR]= 1.18, $p < .01$) such that older age was significantly correlated with completing treatment for A-A ($r = .23$, $p = .02$) but not for White adults ($p = .28$). In Sample #2, treatment completion was significantly associated with age ($OR = 0.95$, $p < .01$) such that older adults were less likely to complete treatment, but was not associated with race or the interaction of race and age.
Conclusions: In contrast to prior results, completion of substance abuse treatment in "real-world" community settings was not poorer for A-A vs. White adults with primary marijuana use; in fact, some older A-As may show higher rates of treatment completion. In spite of treatment completion, older vs. younger adults may not derive the same benefit from treatment, regardless of race. Future studies should explore the relationship between age and marijuana treatment outcome given the mixed findings of the current research.
Financial Support: Supported by FRI and UAB internal funds, R01CA141663, R34 DA031936 & U01 DA031515-03S1.

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WHEEL RUNNING DOSE DEPENDENTLY ATTENUATES COCAINE-SEEKING AND ASSOCIATED NEUROADAPTATIONS IN THE PREFRONTAL CORTEX.

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Aims: Aerobic exercise has been suggested as a potential treatment for cocaine addiction. We recently showed that 2 hrs/day of wheel running, an animal model of aerobic exercise, was sufficient to attenuate subsequent cocaine-seeking and associated neuroadaptations in the prefrontal cortex (PFC). The goal of the current study was to identify the running wheeling conditions that produce the most efficacious response, and given recent findings implicating the promotor IV region of BDNF in cocaine-seeking, an additional goal was to determine whether wheel running dose-dependently modified this region of the BDNF gene in the PFC.
Methods: Once male rats (N=45) acquired cocaine self-administration, they were given extended access (ExA) to cocaine (1.5 mg/kg/infusion) under a discrete trial procedure (4 infusions/hr, 24 hr/day) for a total of 10 days. Following ExA self-administration rats began a 14 day abstinence period wherein they had 1, 2, or 6 hr/day access to a locked or unlocked running wheel. Cocaine-seeking, as assessed under a cued-induced reinstatement paradigm, was then examined after the 14th day of abstinence. PFC punches were removed and BDNF promoter IV mRNA expression was examined by qPCR.
Results: Prior to abstinence and wheel assignment all rats had similar cocaine intake over the 10 day ExA period. Rats given longer wheel running access ran significantly more than rats given shorter access. Levels of cocaine-seeking progressively decreased with increasing levels of access to an unlocked running wheel. ExA cocaine self-administration induced a significant increase in BDNF-IV expression in the PFC when compared to saline controls, and this increase was attenuated by wheel running, particularly in the 6 hr group.
Conclusions: Taken together, these data suggest that wheel running dose-dependently attenuates cocaine-seeking by blocking changes in BDNF promoter IV mRNA expression in the PFC.
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VARIATION OF SERUM BDND LEVELS IN ADOLESCENT CRACK-COCAINE ABUSERS AFTER 20 DAYS' ABSTINENCE.

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Aims: Our aim was to evaluate if there is a change in periferic blood Briain - Derived-Neurotrophic Factor (BDNF) levels after a period of abstinence in adolescent crack cocaine abusers
Methods: A consecutive sample of Adolescents (12-17 years and 11 months) was collected in two inpatient wards in the city of Porto Alegre, in the south of Brazil. All patients and either one of the parents or legal guardian gave informed written consent for participation. A blood sample was collected at baseline (up to 72h after admission) and right before discharge, 20 days later. BDNF levels were measured through Enzyme Linked Immuno Sorbent Assay (ELISA), according to the instructions provided by the kit's manufacturer. Patients were evaluated by administration of the Kiddie-Schedule for Affective Disorders and Schizophrenia, Present-Lifetime version (K-SADS-PL) and later clinical evaluation by a child psychiatrist. Statistical analyses where made using Student's t test for paired samples, since the distribution was normal, and a level of significance of 5% was used for all the analyses. All analyses were made in SPSS program version 17.0.
Results: A total of 62 subjects were included in the study. There was a significant difference on BDNF levels between the baseline and the 20-day abstinence sample (means = 26.929 vs 31.763ng/ml, p=0.007).
Conclusions: A period of abstinence of crack use in a closed ward seem to increase BDNF levels in adolescent crack users. That might be an indicator of neuroadaptation during that period. Further studies are needed to asses whether this implies in better prognosis for recovery, or is a predictor of relapse.
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EMOTION REGULATION PREDICTS DRUG USE AMONG COLLEGE BINGE DRINKERS.

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Aims: Binge drinking among college students represents an important public health concern, and illicit drug use is significantly elevated in this population and accounts for incremental risk. Consistent with the Affective Motivational Model, (Baker et al., 2004), in which negative affect is central to motivating drug use, difficulties regulating one's emotions may be a risk factor for engaging in illicit drug use and developing subsequent drug-related problems among this vulnerable population. The present research examined the hypothesis that difficulty regulating one's emotions would account for drug use after controlling for other established risk factors (i.e., gender, ethnicity, and impulsivity).
Methods: Participants were 207 college students who reported one or more binge episodes (defined as having 4/5 drinks or more on one occasion for women/men) in the past month. Participants reported on illicit drug use in the past six months, days of marijuana use in the past 30 days, and drug-related problems. They also completed a delay discounting measure and the Difficulties in Emotion Regulation Scale (DERS).
Results: Hierarchical multiple regression was used to assess the ability of the DERS to predict number of illicit drugs used in the past six months. After controlling for the influence of gender, ethnicity, and delay discounting, poorer emotion regulation (ER) significantly predicted greater number of illicit drugs used, ΔR^2 =.033, $F(4,194)=3.32$, p=.01. A separate hierarchical multiple regression was used to assess the ability of the DERS to predict drug-related problem severity. After controlling for the influence of gender, ethnicity, and days of marijuana use in the past month, poorer ER significantly predicted greater drug-related problems, ΔR^2 =.10, $F(4,112)=13.13$, p<.001.
Conclusions: Difficulty regulating one's emotions represents a significant risk factor for illicit drug-related problems among college binge drinkers and may be an important target for interventions aiming to decrease college student drug use.
Financial Support: Alcohol Research Foundation (ABMRF)

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MAKE YOUR OWN CIGARETTE SMOKING:TOXICANT EXPOSURE AND BEHAVIORAL CHANGES.

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Aims: Increased price of factory made (FM) cigarettes have led to dramatic increases in the use of make your own (MYO) cigarettes, however, behavior changes and toxicant exposure associated with MYO use have not been evaluated.
Methods: Six FM smokers (4 men) experimentally switched to exclusively smoking MYO cigarettes for 15 days. Cigarettes were made using a machine to inject loose tobacco into preformed filtered cigarette tubes, PMM. At Visit 1 (V1), their usual FM cigarette was smoked through a puff topography instrument; heart rate (HR), carbon monoxide (CO), and blood samples were taken before and after smoking. Participants were instructed how to make PMMs using a provided machine, tobacco, and tubes. Thereafter, participants made and exclusively smoked PMM. At each subsequent lab visit (3; approximately 4 days apart), they made 5 PMMs and smoked one through the topography unit.
Results: Cigarettes smoked per day were the same (22) with FM and PMM. Participants became efficient producers of PMMs as evidenced in the reduced time to make 5 PMMs in the lab (377 sec at V1 to 211 sec at V4). Participants reported it easy and enjoyable to make and smoke PMMs, however the PMM cigarettes (0.78 g) were significantly smaller (p<0.01) than their usual FM cigarettes (0.94 g). Over all conditions, nicotine plasma levels averaged 18.0± 2.4 ng/ml before smoking and 34.0 ± 5.3 ng/ml after smoking; there were no significant differences in the plasma nicotine boost (average 17.7 and 15.4 ng/ml after FM and PMM smoking, respectively). Compared to the V1 FM cigarette, the PMMs were smoked faster and with more puffs, averaging higher puff volumes and velocitiest. Compared to the FMs, the PMMs at V3 (p<.05) and V4 (p<.10) caused higher HR boost (4 bpm vs. 8 bpm) and lower CO boost (7.3 vs. 4.1 ppm; p<0.05). Participants progressively accepted the PMM cigarettes, however, one month after the study none were smoking PMM.
Conclusions: This study demonstrated FM smokers can readily adopt PMM preparation. Smoking PMM cigarettes exposes users to similar levels of nicotine with reduced CO.
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METHAMPHETAMINE SELF-ADMINISTRATION IN HUMANS DURING D-AMPHETAMINE MAINTENANCE.

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Aims: Translational research suggests that agonist replacement may be a viable treatment approach for managing stimulant use disorders. This study sought to determine the effects of d-amphetamine maintenance on methamphetamine self-administration in stimulant using human volunteers. We predicted d-amphetamine maintenance would reduce methamphetamine self-administration.
Methods: Eight volunteers completed the protocol that tested two d-amphetamine maintenance conditions in counter-balanced order (0 and 40 mg/day). Volunteers completed 4 experimental sessions under each maintenance condition in which they first sampled one of four doses of intranasal methamphetamine (0, 10, 20, or 30 mg). Volunteers then had the opportunity to respond on a computerized progressive ratio task to earn portions of the sampled methamphetamine dose. Subject-rated drug-effect and physiological measures were completed at regular intervals prior to and after sampling methamphetamine.
Results: Methamphetamine was self-administered as an orderly function of dose regardless of the maintenance condition. Methamphetamine produced prototypical subject-rated effects, some of which were attenuated by d-amphetamine maintenance. Methamphetamine was well tolerated during d-amphetamine maintenance and no adverse events occurred.
Conclusions: Although d-amphetamine attenuated some subject-rated effects of methamphetamine, the self-administration results are concordant with those of a clinical trial showing that d-amphetamine did not reduce methamphetamine use. Human laboratory self-administration studies can be used to screen other putative agonist replacement pharmacotherapies prior to clinical trial testing.
Financial Support: NIDA R01 DA025032 (PI: CRR)

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GENDER, PROBLEM-GAMBLING SEVERITY, AND THE INCIDENCE OF SUBSTANCE USE DISORDERS.

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Aims: To investigate whether the prospective association between problem-gambling severity and incident substance use disorders (SUDs) differed in women compared to men. In cross-sectional data, pathological gambling (PG) is more strongly associated with SUDs in women versus men; thus, we hypothesized that incident SUDs (both as a group and as relating to alcohol-, tobacco- and other drug-use disorders) would follow the same pattern.
Methods: Wave-1 and Wave-2 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) data from 34,006 non-institutionalized US adults were analyzed. Wave-1 participants were categorized as non-gambling/low-frequency gambling (NG/LFG), low-risk gambling (LRG), and at-risk/problem gambling (ARPG) based on the ten inclusionary criteria for pathological gambling (PG). Dependent variables were any substance-use disorder (SUD), alcohol abuse/dependence (AUDs), nicotine dependence (ND), and drug abuse/dependence (DUDs).
Results: Gender moderated the effects of problem-gambling severity on incident ND and DUDs, with effects stronger in women relative to men. Among women, LRG (OR=1.38; p=.0037) and ARPG (OR=2.14; p=.0023) were associated with elevated odds for ND, relative to LFG/NG; odds were not elevated in men (LRG: OR=1.02; p=.79; ARPG: OR=0.95; p=.84). While the gender difference in DUDs at the level of LRG was significant (Interaction OR= 1.90; p=.028), the gender-specific relationships between LRG and DUDs were not (women: OR=1.31; p=.24; men: OR=0.69; p=.05). Incident AUDs in relation to ARPG followed a distinct pattern, with associations observed in men (OR=2.27; p=.0008) but not women (OR=1.02; p=.96).
Conclusions: Study findings highlight the relevance of considering gender in the prevention and treatment of SUDs. Those factors underlying the progression of specific SUDs in women and men with greater problem-gambling severity warrant identification, particularly as incident AUDs as compared to ND and DUDs showed gender-related differences that differed from cross-sectional patterns.
Financial Support: Supported by grants from NIMH, NIDA, and NCRG

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ASSOCIATION BETWEEN AAS USE, MUSCLE DYSMORPHIA AND ILLICIT DRUG USE AMONG GYM FREQUENTERS.

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Aims: The use of anabolic-androgenic steroids (AAS) has increased among gym frequenters. Many people are involved in strength training to enhance their appearance, but this population might be at higher risk for of use of external ergogenic substances to achieve the muscular development desired. The aim of this study was to evaluate the prevalence of AAS use among gym frequenters and associated factors, such as muscle dysmorphia and illicit drugs.
Methods: In a cross-sectional study, from a consecutive and proportional sample (n=278) of adult gym frequenters, in the South of Brazil, anonymous questionnaires were self-completed by adults.
Results: The prevalence of AAS use was 9.7%. It was found a strong association between AAS use and distorted body self-image (PR=6.33; p ≤0,01; CI95% 2.42-16.55) and with other illicit drugs such as marijuana/cocaine use (PR=4,80, p=0.03, CI95% 1.08-21.21).
Conclusions: There was a high prevalence of AAS use among gym frequenters. Our results indicate that AAS use is not a healthy behavior, as usually suggested in the media, linking muscles with health. On the contrary, AAS was associated to self–destructive behavior -marijuana and cocaine. Corroborating this idea, it was not a surprise the strong association between AAS use and distorted self-image, an indicative of their exaggerated concern with the appearance of their muscles. We can understand these individuals as a special vulnerable group, usually involved with other destructive behavior, who will use any external way to achieve the desired shape, even if they have to disregard the substantial health.
Financial Support: none

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DRUG USE TRENDS FOLLOWING THE 12-WEEKS OST IN THE REPUBLIC OF GEORGIA (RCT).

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Aims: Aims: To obtain data on the acceptability and impact on drug use and HIV risk achieved by a 12-week course of daily-observed Suboxone® or methadone among opioid addicted Subutex® injectors.
Methods: Methods: Randomized controlled 12-week trial of daily-observed methadone or buprenorphine-naloxone with weekly counseling.
Weekly urine tests on opioids, amphetamines, benzodiazepines and marijuana, and self-reports (TLFB); ASI at weeks 0, 4, 8, 12, 20.
Results: Results: Of the 80 patients (40/group, 4 women), 68 (85%) completed the 12-week study treatment and 66 (82.5%) showed up for the 20-week follow-up. 68.4% participants in methadone group and 72.5% in Suboxone® group reported injecting more than one illicit drug in last 30 days prior to randomization. Illicit drug use was dramatically reduced during the treatment (weeks 1-12) with significantly more urine samples positive for opioids in methadone group (1.5% vs. 0.2%; p=0.03), for amphetamines (2.8% vs. 0.2%; p<0.001) and marijuana (10.2% vs. 1.7%; p<0.001)- in Suboxone® group (1-12 weeks). Of 836 urine test results and TLFB responses obtained during 1-12 weeks, 96.7% were in agreement. At follow-up (week 20) assessment (n=66), participants remaining in OST (n=37; 46%) used significantly less opioids (5.6% vs 27.6%; p<0.001), less illicit buprenorphine (2.7% vs 13.8%; p=0.005) less benzodiazepines (13.5% vs 34.5%; p<0.001), and less marijuana (2.8% vs 20.7%; p<0.001), compared to those who left the treatment.
Conclusions: Conclusions: OST with daily observed methadone or buprenorphine-naloxone and weekly counseling is effective for reducing opioid and other psychoactive substances use in the Republic of Georgia.
Financial Support: R21-DA-026754-NIDA

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THE NK1 ANTAGONIST APREPITANT REDUCES STRESS-INDUCED COCAINE AND ALCOHOL CRAVING IN A HUMAN LABORATORY STUDY.

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Aims: Initial studies of Neurokinin 1 (NK1) antagonism demonstrated reductions in stress-induced alcohol craving. This study extended such invesitigations to stress-induced cocaine and alcohol craving using the NK1 antagonist Aprepitant.
Methods: Non-treatment seeking adult cocaine and alcohol dependent subjects (n =12) were enrolled in a four-session outpatient human laboratory study. Subjects received placebo or Aprepitant in each of two sessions using a psychological stressor, and in each of two session using a physiologic stressor. During each session, measures of cocaine and alcohol craving were gathered both pre- and post-stressor.
Results: Compared to placebo, Aprepitant significantly reduced cocaine craving during the physiologic stress sessions, as measured using the Cocaine Craving Questionnaires (CCQ). These craving reductions were driven by subjects' decreased expectations about positive outcomes from cocaine use, and occurred at multiple timepoints post-stressor (ps < .05). Compared to placebo, Aprepitant also reduced alcohol craving during the physiologic stress sessions, as measured by the Alcohol Craving Questionnaire (ACQ). These craving reductions were driven by subjects' decreased expectations about relief of withdrawal from drinking, and occurred at multiple timepoints post stressor (ps = .05). There were no parallel reductions in cocaine or alcohol craving during the psychological stress sessions.
Conclusions: These results demonstrate that the NK1 antagonist Aprepitant reduced stress-induced cocaine and alcohol craving under conditions of physiological stress, but not under conditions of psychological stress. The reductions in cocaine craving relate primarily to decreases in expectations about positive outcomes from cocaine use. In contrast, reductions in alcohol craving relate to decreases in expectations about relief from withdrawal or dysphoria. Taken together, these suggest that Aprepitant may have a different mechanism of action in alcohol dependence and in cocaine dependence.
Financial Support: Support for this study was provided by P50DA012756 and K01DA025073

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DNA METHYLATION IS ALTERED WITH EXTENDED ACCESS TO COCAINE DURING ABSTINENCE.

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Aims: DNA methylation is a key determinant of gene expression and is implicated in neuroplasticity relevant to addiction. Here, we examine DNA methylation within the dorsal medial prefrontal cortex (dmPFC) following limited- or prolonged-access to cocaine self-administration and varying periods of forced cocaine abstinence.
Methods: Rats were fitted with IV catheters and allowed to lever press for saline, limited-access (1h/day) to cocaine, or prolonged-access (6h/day) to cocaine for 15 sessions. Then, dmPFC was collected at either 1, 14, or 60 days of abstinence from self-administration. As reported previously, only prolonged-access rats exhibited escalated cocaine intake across sessions and had intake substantially higher than the limited-access group. MeDIP-CHIP and qPCR analyses of dmPFC tissue revealed dramatic and extremely gene-specific changes in DNA methylation/demethylation within promoter regions and flanking the transcription start site (TSS) across groups.
Results: The region flanking TSS in the gene Npas4 exhibited dynamic changes in DNA methylation following limited and prolonged-access that varied in response to treatment as well as length of abstinence. After 1 day of abstinence, the prolonged-access group was trending towards increased methylation at TSS, at 14 days after treatment only the prolonged-access group exhibited decreased methylation surrounding TSS, whereas after 60 days post-treatment there was a reversal and the limited and prolonged access groups exhibited dramatically increased methylation from the control.
Conclusions: These results demonstrate that cocaine self-administration alters DNA methylation dynamically over the course of abstinence, as well as the transcription of mRNA in both limited and prolonged access to cocaine. The present findings provide a possible molecular mechanism mediating the enduring nature of cocaine addiction during abstinence.
Financial Support: The research was supported by grants from NARSAD and NIH (R21DA027115).

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THE IMPACT OF STATE-LEVEL EDUCATION POLICY, TAXATION, INCOME DISPARITY AND POLITICAL IDEOLOGY ON TOBACCO USE IN TWO NATIONALLY REPRESENTATIVE SAMPLES.

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Aims: Math and science education may be linked to improved health decision making. State-by-state increases in graduation requirements in the mid '80s and early '90s offer an opportunity to explore this potential effect. To this end, we used two nationally representative samples to examine the effects of higher math and science coursework requirements on smoking initiation, defined as ever smoking 100 cigarettes; we also included several state-level covariates that could affect education quality and funding: cigarette tax rate, political ideology and income disparity.
Methods: Four waves (1999, 2001, 2003 and 2006) of the Tobacco Use Supplement of the Current Population Survey (TUS-CPS) and eleven administrations (1998-2008) of the Behavioral Risk-Factor Surveillance System (BRFSS) were paired with state-level graduation requirement data. Analyses were conditioned on high school graduation; 16,364 TUS-CPS and 54,661 BRFSS respondents met inclusion criteria and graduated during the period of interest (1980 to 1999). Logistic regression was used to model the effect of graduation requirement on smoking initiation.
Results: Higher math and science graduation requirements were associated with lower odds of smoking initiation for both samples, which persisted after including additional state-level covariates and in stratified analyses based on race/ethnicity and sex. Associations for whites of both sexes were likely driving results for the full samples, although confidence intervals for all subgroup analyses overlapped. For example, white BRFSS respondents who were exposed to the highest requirements were at 8% lower odds to have initiated smoking compared to those with the lowest requirements (OR = .92, CI [.87, .95], p < .001).
Conclusions: Our findings support a significant association between increasing math and science education at the high school level and smoking initiation, independent of further educational attainment and state-level characteristics such as cigarette taxation, income disparity and political ideology.
Financial Support: NIDA T32DA07313, K02DA021237, R21DA026 and R01DA031288.

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CLEARING THE SMOKE ON CANADIAN YOUTHS' PERCEPTIONS OF CANNABIS.

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Aims: Given the high prevalence of cannabis use among Canadian youth, this study aimed to explore youths' perceptions of its use and misuse. The study specifically examined youth perceptions of how decisions about cannabis use are influenced by family, peers, community, the law and the medical use of cannabis.
Methods: Qualitative data were collected from 76 youths aged 14-19 years during two online and 10 in-person focus groups conducted in five cities across Canada. The sample included 34 (45%) junior youths (aged 14-15 years) and 29 (38%) females. All data were analyzed using thematic analysis.
Results: The focus group participants indicated that decisions to use cannabis are influenced by a variety of factors within their family, community and social networks. The focus groups also revealed a strong belief that all young people are using cannabis daily. The youths cited concerns about health risks, poor academic performance and negative effects on familial relationships as key influences on the decision not to use cannabis. They expressed frustration and confusion about inconsistency in police reactions to cannabis and had difficulty positioning the role of medical cannabis in their understanding of the legal context. Moreover, the participants perceived the medical use of cannabis to represent a double standard in which cannabis is good for you if you are sick, but not if you are healthy. They downplayed the potential negative effects of cannabis and argued that negative effects should be attributed to the individuals experiencing problems, rather than to cannabis itself.
Conclusions: This research identified a number of factors that the participants perceived as influential in affecting decisions to use cannabis or not. The results highlight the complexity of youth perceptions of cannabis and point to the challenges associated with preventing the use and abuse of this illicit substance. Mixed messaging and the increasingly apparent complacency surrounding cannabis use among youths are areas in need of further investigation.
Financial Support: This research was supported by a financial contribution from Health Canada's Drug Strategy Community Initiatives Fund.

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BUPRENORPHINE AND METHADONE MAINTENANCE TREATMENT OUTCOMES FOR OPIOID ANALGESIC, HEROIN, AND COMBINED USERS: FINDINGS FROM STARTING TREATMENT WITH AGONIST REPLACEMENT THERAPIES (START).

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Aims: This secondary analysis explored differences in baseline characteristics and opioid replacement therapy (ORT) treatment outcomes by type (heroin, opioid analgesic (OA), combined) and route (injector, non-injector) of opioid use.
Methods: 1269 participants were randomized to receive methadone or buprenorphine for 24-weeks; 731 completed treatment. Outcomes were opioid use during the final month of treatment, among treatment completers, and attrition.
Results: Non-opioid substance dependence diagnoses and injecting differentiated heroin and combined users from OA users. Non-opioid substance dependence diagnoses and heroin use differentiated injectors from non-injectors. Injectors were more likely to be using at end of treatment compared to non-injectors. OA users were more likely to complete treatment than heroin (65.3% vs. 55.3%) and combined (57.9%) users. Non-injectors were more likely than injectors to complete treatment (63.6% vs. 54.9%). There were no interactions between type of opioid used or injection status and treatment assignment on opioid use or treatment attrition.
Conclusions: Substance use severity differentiates heroin users from OA users and injectors from non-injectors. Irrespective of ORT medication, heroin use and injecting are associated with treatment attrition and opioid misuse during treatment. These results are of particular interest clinically as there is no evidence of superiority of buprenorphine over methadone for treating OA users versus heroin users.
Financial Support: Grant Funding for this study was provided by NIDA Clinical Trials Network Grants U10 DA020024 (Trivedi), U10 DA13045 (Ling), 5 U10 DA013714-08 (Donovan/Roll), U10 DA13036 (McCarty), and K23 DA02297 (Potter).

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REDUCED ANTINOCICEPTION OF OPIOIDS IN RATS AND MICE BY VACCINATION WITH IMMUNOGENS CONTAINING OXYCODONE AND HYDROCODONE HAPTENS.

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Aims: Prescription opioids abuse and associated deaths are an emerging concern in the USA. Vaccination against prescription opioids may provide an alternative to pharmacotherapy. An oxycodone hapten containing a tetraglycine linker at the C6 position (6OXY(Gly)4OH) conjugated to the carrier protein keyhole limpet hemocyanin (KLH) has shown early proof-of-efficacy in rodents as a candidate immunogen (6OXY(Gly)4-KLH) for the treatment of oxycodone abuse.
Methods: In this study, oxycodone-based and hydrocodone-based haptens were conjugated to KLH through amide and thioether coupling chemistry to generate immunogens that would recognize both oxycodone and hydrocodone. Immunogens were evaluated in mice and rats.
Results: Vaccination with 6OXY(Gly)4-KLH increased drug binding in serum, reduced drug distribution to brain and blunted analgesia for both oxycodone and hydrocodone. An analogous C6-linked hydrocodone vaccine blocked hydrocodone effects but less so than 6OXY(Gly)4-KLH. C8-linked hydrocodone immunogens had only limited efficacy. Amide conjugation showed higher haptenation ratios and greater efficacy than thioether conjugation to maleimide activated KLH (mKLH).
Conclusions: The 6OXY(Gly)4-KLH vaccine may be used for treatment of prescription opioid abuse. Vaccination did not prevent fentanyl analgesia suggesting that pain management is possible in vaccinated individuals.
Financial Support: NIH NIDA DA026300 (Pentel) and by a Minneapolis Medical Research Foundation Career Development Award (Pravetoni).

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INFLUENCE OF ORGANIZATIONAL AND STAFF CHARACTERISTICS ON SUCCESS IN IMPLEMENTING PROCESS IMPROVEMENT GOALS IN CORRECTIONAL TREATMENT SETTINGS.

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Aims: The Organizational Process Improvement Intervention study, one of NIDA's CJDATS studies, is examining a Change Team and Facilitator strategy to improve offender assessment, case planning, and referral to community treatment for substance-abusing offenders. The research question addressed is: Which organizational characteristics and staff attitudes are related to the ability of Change Teams to achieve planned improvements in assessment and case planning processes in correctional and community treatment settings?
Methods: The independent variables were factor scores from a principal component analysis of a baseline survey of organizational characteristics administered to staff. The PCA yielded five factors: Organizational Climate, Efficiency/Growth, Organizational Needs, Resources, and Support for Evidence-Based Practices (EBP). The dependent variable was a rating of the degree to which each Change Team site was successful in achieving its goals related to assessment and case planning. Sites fell into three levels of success (Low, Medium, High). GLM analysis was used to determine which of the factor scores were associated with success in achieving goals. Post-hoc analyses determined how pairs of success levels differed in factor scores.
Results: The three Success categories differed significantly on the five factors ($p < .001$). Two of the factors were significantly associated with Success: Resources ($p < .001$) and Support for EBP ($p = .01$). In post-hoc analyses, the High Success category had significantly higher factor scores on Resources and Support for EBP compared with the Medium and the Low Success categories. The Medium Success category had a higher factor score on Support for EBP than the Low Success category.
Conclusions: Success in achieving goals by Change Teams appears to be more likely in those sites where staff have higher levels of resources and exhibit greater support for EBP.
Financial Support: NIDA, SAMHSA, BJA

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DIFFERENTIAL RISK OF RACIAL ADMIXTURE FOR SUBSTANCE ABUSE: A LONGITUDINAL ANALYSIS.

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Aims: Racially-admixed adolescents are at higher risk of substance use and abuse; however, findings from cross-sectional adult populations are inconsistent. We use prospective national data to (1) test an "adolescent-limited" hypothesis of substance abuse in mixed, relative to non-mixed adolescents and (2) identify factors that may explain the differential trajectories.
Methods: Three waves of the National Longitudinal Study of Adolescent Health (Add Health) data were analyzed for Asian American and Pacific Islanders (AAPI) and African Americans (AA) among those participated in all three waves (N=11,621). Adolescents were 7-12th grade at Wave 1 (W1, 1994-5). Wave 2 (W2) was conducted in one year later, and Wave 3 (W3) in 2001-2. Cumulative marijuana use and excessive drinking in past year were included for comparisons with our previous cross-sectional data. AAPI (n=938) and AA (n=2611) groups were analyzed separately; and mixed race group was respective racial origin mixed with any other race. Mixed model repeated measures ANOVA was used to answer specific aims.
Results: Weighted and variance-adjusted risk ratios (RR) of the marijuana prevalence of the mixed vs. non-mixed AAPIs were 2.86 (W1), 2.77 (W2) and 2.10 (W3) ($p<.0002$ for all waves); RRs for excessive drinking were 2.37, 2.93, 1.59, respectively ($p<.004$, W2 only). The overall difference of mixed vs. non-mixed marijuana use was significant ($p<03$), but not overtime change ($p=.10$), while controlling for main measures (e.g., age, gender, being mixed, antisocial behaviors, college aspiration, sexual behavior, parent and proband foreign born (all but one, $p<.0001$)). For excessive drinking, only W1 differences were significant. Being mixed-race, probed, foreign-born, and college aspiration were non-significant. Increased risk for mixed AAs were more modest than AAPIs; the difference was significant only at W3. Multivariate results showed being-mixed was overall significant.
Conclusions: The adolescent-limiting hypothesis was supported for excessive drinking among AAPIs only.
Financial Support: R01DA020922, T32DA007313

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ASSOCIATION OF CHILDHOOD SEXUAL AND OTHER PHYSICAL ABUSE WITH LIFETIME AND PRENATAL DRUG USE IN URBAN AFRICAN-AMERICAN WOMEN.

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Aims: To estimate the degree of association linking earlier sexual and other physical abuse in childhood with drug and alcohol use and other risk behaviors in urban African-American women.
Methods: Data were drawn from the Miami Prenatal Cocaine Study postpartum survey of urban, low SES, African-American women (18 years or older) delivering at UM-Jackson Memorial Hospital in the early 1990's. Maternal self-report of having been abused physically or sexually during childhood was analyzed in relation to lifetime and prenatal use of alcohol and drugs (self-report and bioassays). Analyses included Student t-tests, Chi-square, and Wilcoxon rank sum.
Results: Among the mothers (mean age, 25 yrs; 88% single), 353 (24%) reported having been exposed to sexual (15%) or other physical (17%) abuse during childhood (<18 years). Mothers with childhood abuse were significantly more likely ($P<0.05$) to have used alcohol, tobacco, marijuana, and cocaine/crack (ever and during pregnancy); to have engaged in risky sex; and to have been arrested/charged.
Conclusions: This study adds to growing evidence linking childhood trauma (here, sexual and other physical abuse) with later risk behaviors, including drug involvement. It is one of the few studies to report on the degree to which earlier childhood trauma might account for prenatal drug use (measured by postpartum self-report and bioassays), known to pose serious risks to mothers and their offspring. These findings suggest that interventions to reduce childhood trauma might prevent or ameliorate later drug use during pregnancy.
Financial Support: NIDA & Office of Research on Women's Health P50DA024584; R01DA006556; K01DA016720; K05DA15799; Public Health Springboard Grant, University of Miami Miller School of Medicine, Dept. of Epidemiology & Public Health; UM D-CFAR

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DOSE-DEPENDENT PHYSIOLOGICAL AND SUBJECTIVE EFFECTS OF MARIJUANA IN DAILY MARIJUANA SMOKERS.

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Aims: Smoked marijuana (MJ) produces a wide range of subjective and physiological effects including tachycardia and intoxication. Demonstrating that these effects are dose-dependent is important for understanding how potential treatment medications shift MJ's effects. The present within-subject, double-blind study was designed to develop a MJ-smoking procedure to reliably obtain a dose-response function for MJ's effects.
Methods: During each of the 4 outpatient sessions, non-treatment seeking, daily MJ smokers (N = 17M, 1F) smoked six 5-second puffs from 3 MJ cigarettes (2 puffs from each cigarette). The number of puffs from active (≥ 5.5% THC) and inactive (0.0% THC) MJ cigarettes smoked during each session varied according to condition (0, 2, 4, or 6 active puffs); active puffs smoked before placebo puffs. The subjective, physiological and psychomotor-task performance effects of MJ as a function of puff condition ('dose') were assessed at timed intervals prior to and after MJ administration.
Results: Active MJ dose-dependently increased heart rate and decreased carbon monoxide expiration ($p \leq 0.001$), an index of inhalation strength. Active MJ also increased subjective ratings of marijuana 'Strength,' 'High,' and positive subjective-effect ratings such as 'Liking,' 'Good Effect' and 'Take Again' ($p \leq 0.001$) compared to inactive MJ, but these effects were not dose-dependent. Active MJ also produced modest deficits in attention, psychomotor function and recall relative to inactive MJ.
Conclusions: These findings demonstrate that the dosing procedure elicited dose-dependent cardiovascular effects even though participants inhaled less as MJ dose increased. Yet, most subjective ratings of marijuana intoxication did not vary as a function of dose. We hypothesize that participants' expectation of MJ intoxication makes it difficult to detect dose-dependent differences in subjective drug effects. Thus, controlled investigations of MJ's effects need to control for the likely contribution of expectancy effects.
Financial Support: Supported by NIDA Grant DA19239

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TWITTER: A WINDOW ON ALCOHOL USE?

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Aims: Recent innovations in social networking have generated new sources of information for behavioral scientists. The available literature on Twitter explores methodologies to mine Tweets for sentiment and how accurately that content predicts behavior, such as stock market trends or public safety (Bollen et al., 2010; Mao et al., 2011). Few studies have examined Twitter as a source of health-related information. Golder and Macy (2011) investigated the frequency of positive or negative affect tweets across the span of a day, week, month, and year and found that the Twitter data was consistent with the existing literature regarding mood and circadian rhythms. Our study explores Twitter's application to public health concerns and aims to determine whether such data is a viable methodology for the behavioral sciences.
Methods: Data consisted of approximately nine months of randomly sampled Twitter data, or tweets, from English-speaking users. The average age of Twitter users is 31 years old, with a majority of users falling in the 18-49 age range (Fox et al., 2009). TopicWatch, a Twitter analytics program developed by the company LuckySort, was used to examine the frequency of tweets regarding self-referent drinking behavior across time.
Results: In a randomly selected day, peaks in drinking-related tweets occurred during 8:00 PM and 10:00 PM. Consistent with Goldman et al. (2011), the highest occurrences of self-referent tweets containing "drunk" in a given week were on Saturdays. Further, holidays and special events across this period showed spikes in self-referent tweets focusing on drunkenness, including SuperBowl Sunday, St. Patrick's Day, Cinco de Mayo, July 4th, and Thanksgiving.
Conclusions: This investigation suggests that Twitter may be a viable methodology for examining public health phenomenon. These findings begin to reflect the potential efficacy of social networking platforms as a means of assessing large populations. The congruence of Twitter self-report data with empirically supported alcohol use patterns is encouraging in its implications for future prevention methods.
Financial Support: None

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CALIFORNIA SMOKIN': TOBACCO AND MARIJUANA USE AMONG YOUNG ADULTS IN CALIFORNIA COMPARED TO THE REST OF THE U.S.

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Aims: Californians are more likely to smoke marijuana (MJ) and less likely to smoke tobacco (TOB) compared to most other states in the US. The current study examined young adults' co-use of tobacco and marijuana and their thoughts about quitting.
Methods: Young adults age 18 to 25 (N = 1987) across the US who had smoked at least one cigarette in the past month completed an online anonymous survey. More than half (53%) had used MJ in the past 30 days. Controlling for age, gender, ethnicity, household income, and urban/rural area, linear and logistic regressions compared 3 location groups on TOB and MJ variables: 1) California; 2) states with legal medical MJ programs (medMJ); and 3) states without a medical MJ program (no-medMJ).
Results: Controlling for demographic differences, compared to medMJ and no-medMJ states, Californians used TOB less frequently and less intensely (21 days/mo vs. 23 for other 2 groups; $p<.01$; 3.8 cigs per day vs. 5.3 medMJ, 6.2 no-medMJ; $p<.01$; 57% daily smokers vs. 70% medMJ vs. 71% no-medMJ; $p<.01$). MJ use was more prevalent in California than other states (59% vs. 53% medMJ, 52% no-medMJ; $p<.05$). Compared to the other two groups, Californians had less positive expectancies regarding TOB use ($p=.03$) and anticipated greater success with quitting TOB ($p<.01$). There were no significant differences on TOB or MJ readiness to quit, % days using both TOB and MJ, abstinence goals, or thoughts about MJ abstinence.
Conclusions: Young adult smokers living in California smoked TOB less frequently and intently and anticipated greater success with quitting smoking relative to other states. They were more likely to use MJ but rates of TOB/MJ co-use did not differ. Further, findings suggested comparable thoughts about MJ use and quitting among young adult smokers irrespective of the medical MJ policy in their state.
Financial Support: TRDRP; 18FT-0055; PI, D. Ramo

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TOPIRAMATE IMPAIRS COGNITIVE FUNCTION IN COCAINE-DEPENDENT INDIVIDUALS MAINTAINED ON METHADONE.

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Aims: Topiramate is being investigated as a potential pharmacotherapy for the treatment of addictive disorders. However, its cognitive side effects raise concerns about its use, especially in cognitively impaired populations such as persons with substance use disorders. The purpose of this study was to assess the cognitive effects of topiramate in individuals dually dependent on cocaine and opioids as part of a double-blind randomized controlled trial of topiramate for the treatment of cocaine dependence.
Methods: Participants were first stabilized on methadone (M=96 mg) for five weeks and trained on a cognitive battery to minimize practice effects, then randomized to topiramate (n=23) or placebo (n=22). Cognitive testing took place at two timepoints: at study week five during the placebo lead-in phase to assess baseline performance, and 10-14 weeks later to assess performance during stable dosing (150 mg topiramate or placebo, b.i.d.). All participants were maintained on methadone at both testing timepoints, and testing occurred two hours after drug administration.
Results: The topiramate and placebo groups did not differ on gender, level of education, premorbid intelligence, or methadone dose (ps > 0.19, t-test or chi-square test as appropriate). A Group (placebo, topiramate) x Time (pre-treatment baseline, stable dosing) mixed design Analysis of Variance (ANOVA) was conducted for each cognitive measure. Significant interaction effects ($p < 0.05$) revealed that topiramate slowed psychomotor and information processing speed (Trail Making Test A, Digit Symbol Substitution Test), reduced working memory accuracy (n-Back), and increased the false alarm rate in episodic memory (word recognition memory). Topiramate had no effects on visual perception, divided attention, or decision-making performance.
Conclusions: The cognitive-impairing effects of topiramate may amplify pre-existing cognitive impairments in substance abusers and limit its acceptability and use as a treatment for substance use disorders.
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THE ASSOCIATION OF IMPULSIVITY AND DISTRESS TOLERANCE WITH PTSD SYMPTOM SEVERITY: A TEST AMONG TRAUMA-EXPOSED, COCAINE-DEPENDENT ADULTS.

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Aims: Despite the well-established comorbidity between PTSD and cocaine dependence, few studies have focused on the role of relevant cognitive and affective factors, such as distress tolerance and impulsivity, that might be targeted in treatment. This study examines the associations between PTSD symptom severity, distress tolerance, and impulsivity among trauma-exposed, cocaine dependent adults. Specifically, it is expected that lower levels of distress tolerance and higher levels of impulsivity will be associated with greater PTSD symptom severity and cocaine dependence severity.
Methods: Participants (N=142) included self-reported cocaine users responding to ongoing recruitment at a large urban cocaine treatment and research center. These participants completed the Addiction Severity Index, Barratt Impulsivity Scale (BIS-11), Posttraumatic Diagnostic Scale (PDS), and Distress Tolerance Scale. Only participants who endorsed trauma exposure on the PDS were included in this analysis.
Results: Among responding participants, 66.9% (n=95) had current cocaine-positive urinalysis results. Distress tolerance ($F(1,109) = 13.21$, $p<.0004$) and impulsivity ($F(1,109) = 4.88$, $p<.0292$) simultaneously demonstrate statistically reliable relations with PDS-defined PTSD total symptom severity and symptom cluster severity. Increased distress tolerance and decreased impulsivity were related to higher levels of PTSD. Data collection is ongoing.
Conclusions: Both distress tolerance and impulsivity demonstrate unique relations with global PTSD symptom severity and symptom cluster severity. Addressing both of these factors has great potential to improve treatment efforts for cocaine-dependent individuals. Relevant treatment implications will be discussed.
Financial Support: National Institute on Drug Abuse Grant P50 DA09262

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DIFFERENCES IN MOOD AND QUALITY OF LIFE INDICATORS BY HIV STATUS IN A GROUP OF METHAMPHETAMINE-DEPENDENT INDIVIDUALS.

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Aims: Individuals who use MA are at increased risk for HIV transmission due to risky sexual behaviors and IV drug use. The co-occurrence of HIV among MA abusing individuals can negatively compound the course of addiction and recovery. This abstract provides information regarding the baseline mood state and quality of life of a sample of HIV positive vs. HIV negative MA abusers in residential treatment who participated in a research study examining the utility of an exercise training program on mood and post-treatment MA use. Data presented here are preliminary and part of an ongoing study.
Methods: Ninety-five MA-dependent individuals were randomized to 3 d/wk of exercise training (EX, n=48) or health education (ED, n=47) over an 8-wk study period. Roughly 65.9% (n=63) of the sample were HIV- and 34.7%, (n=32) were HIV+. Baseline mood was assessed using the BDI & BAI and quality of life was measured with the SF-36.
Results: Participants with HIV were significantly more likely ($p<.001$) to report more hospitalizations in the past year (2.3 times) compared to participants without HIV (1.3). HIV+ clients had significantly more mental health distress compared to HIV- clients as reflected by higher depression mean symptoms on the BDI (15.9, sd=7.7 vs. 11.8, sd=7.9) and higher BAI scores (16.5, sd=14.0 vs. 11.9, sd=12.1) after controlling for demographic and drug use ASI variables. Compared to HIV- participants, those with HIV were more likely to perceive higher dysfunction in the following physical quality of life related scales: physical functioning (91.3 vs. 97.2, $p<.01$), role-physical (62.5 vs. 86.7, $p<.002$), and general health (63.1 vs. 71.2, $p<.05$) as well as significantly poorer mental health functioning in terms of social functioning (55.2 vs. 68.1, $p<.05$), role emotion (35.6 vs. 60.8, $p<.05$), and well-being (51 vs. 61.2, $p<.05$).
Conclusions: Although preliminary, these data underscore the problematic influence of HIV among MA users with regard to negative mood and quality of life indicators such as physical, social and mental health functioning.
Financial Support: NIDA DA027633

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RESTING-STATE BRAIN NETWORKS ARE RELATED TO COCAINE USE IN CHRONIC COCAINE SMOKERS.

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Aims: Functional magnetic resonance imaging (fMRI) research has indicated the involvement of frontal network in cocaine addiction. Resting-state fMRI approaches have revealed reduced (Kelly, 2011; Munier, 2012) as well as enhanced (Camchong, 2011) resting state functional connectivity (RSFC) in frontal network in cocaine users relative to control participants. Also, task fMRI research has identified the insula as an important region activated during cocaine craving (Bonson, 2002). We examined the relationship between resting state networks and measures of cocaine use [frequency, money spent per week; duration] in nontreatment-seeking, chronic cocaine smokers.
Methods: Ten participants (39-53 yrs; 6M;4F) abstinent from cocaine for 72 hrs completed a resting state scan and an anatomical MPRAGE scan. Whole-brain Independent component analysis was performed on resting state fMRI data using FSL's MELODIC program that identified brain networks representing RSFC of frontal-parietal, dorsal-attention, and insula networks. FSL's regression model then determined any correlations between the activity of these brain networks and cocaine use measures.
Results: Activity in frontal-parietal and insula networks was positively correlated with all three outcomes: frequency of use, money spent/week and cocaine use duration. Medial frontal gyrus and inferior parietal lobule [a part of dorsal-attention network (DAN)] positively correlated with each measure. Thus, the increased activity in these brain regions was associated with increased cocaine use.
Conclusions: To our knowledge, this is the first study to demonstrate a relationship between RSFC in frontal and insula networks and measures of cocaine use in chronic cocaine smokers. Relationship between the DAN and cocaine use may suggest increased attentional bias to cocaine cues in the environment. As potential network level biomarkers of chronic cocaine use, these identified resting state networks may be usefully applied in treatment development.
Financial Support: Research supported by NIDA K01DA029047.

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PREVALENCE OF SMOKELESS TOBACCO USE AMONG INDIVIDUALS WITH COMORBID OTHER SUBSTANCE DEPENDENCE.

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Aims: Prevalence of smoking is several-fold greater among individuals with comorbid other substance use disorders compared to those without such problems. A related question that has received relatively little attention and is the purpose of this study is whether comorbid substance use disorders also increase risk for smokeless-tobacco use.
Methods: We examined data from the 2010 National Survey on Drug Use and Health (NSDUH), a multistage area probability sample of U.S. non-institutionalized residents age > 12 yrs, to estimate prevalence of cigarette (past 30 days) and smokeless tobacco use (past 30 days) among individuals age > 18 yrs meeting criteria for either alcohol dependence, cocaine dependence, heroin dependence, or marijuana dependence vs. a sample without dependence other than nicotine/tobacco.
Results: Consistent with prior reports, smoking prevalence was greatest among those meeting criteria for heroin dependence (100%), followed by cocaine dependence (73%), marijuana dependence (69%), alcohol dependence (59%), and those without comorbid substance dependence (28%) ($p < .01$ across all comparisons). Prevalence of smokeless tobacco use was greater among those meeting criteria for alcohol dependence (11.2%, $p < .01$), cocaine dependence (10.7%, $p = .04$), marijuana dependence (9.2%, $p < .01$) compared to those without comorbid substance dependence (4.8%), although those meeting criteria for heroin dependence did not show greater prevalence (7.1%, $p = .56$). The elevations in smokeless tobacco use among those with alcohol or cocaine dependence was evident in both genders and smokers and nonsmokers, while among those with marijuana dependence it was limited to smokers.
Conclusions: While not as robust as the increased risk observed with cigarette smoking, comorbid other substance dependence is associated with a 1.9- to 2.3-fold greater prevalence of smokeless tobacco use, with heroin dependence being a possible exception to this pattern.
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THE EVENT-SPECIFIC ETIOLOGY OF INTIMATE PARTNER VIOLENCE: THE ROLE OF ALCOHOL USE AND PSYCHIATRIC CONDITIONS.

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Aims: Intimate partner violence (IPV) is a public health problem, having been associated with negative outcomes including drug use, physical injury, chronic pain, sexually transmitted diseases, depression, and PTSD. Although studies have examined how drug use and mental health conditions are related to IPV, no studies have assessed the role of event-specific alcohol use, in conjunction with mental health conditions and substance use. The purpose of this study was to examine the prevalence of alcohol use during episodes of IPV. We also sought to understand the independent effects of substance use and mental health on IPV victimization and perpetration.
Methods: Data were obtained from 34,653 adults who participated in the National Epidemiologic Survey on Alcohol and Related Conditions. Event-specific alcohol use was evaluated among any person who experienced some victimization from IPV. Respondents were characterized as having no IPV, being "victims of IPV" only, "perpetrators" only, or "both victim and perpetrator".
Results: Approximately 30% of IPV incidents involved alcohol, and the greatest proportion of those who reported IPV reported that both partners were under the influence of alcohol (14.90%). Alcohol use was most common in mutually aggressive situations in which the respondent was both a perpetrator and a victim of IPV (58% of alcohol users). Quantity of alcohol use was related to victimization (OR=1.08) and victimization and perpetration (OR=1.12). More frequent alcohol use was associated with co-occurring victimization and perpetration (OR=1.71). Marijuana use was strongly associated with victimization only (OR=2.61) and both victimization and perpetration (OR=2.65). Depression, mania, hypomania, panic disorder, specific phobia, and ASPD were related to IPV. PTSD was consistently related to all types of IPV.
Conclusions: Although mental health and substance use frequently co-occur, they appear to have independent effects on dating violence perpetration and victimization.
Financial Support: None.

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A WEB-BASED CONTINGENCY MANAGEMENT PROGRAM WITH ADOLESCENT SMOKERS IN RURAL APPALACHIA.

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Aims: Adolescence represents a challenging but important life period for smoking cessation efforts, and working with rural adolescent smokers can be especially challenging given a number of delivery barriers for rural populations. A web-based contingency management program (CM) for smoking cessation (Dallery et al., 2007) may be particularly useful as a behavioral treatment for rural adolescent smokers. The program can be completed from home using an Internet server and video recordings of breath carbon monoxide (CO) analyses.
Methods: A randomized trial was conducted to compare this CM program to a control-condition program that reinforced timely breath samples with no criterion for breath CO. Sixty four rural Appalachian adolescent smokers participated, with an equal number of participants in each research arm (n = 32). At enrollment, participants across groups did not differ in age, gender, race, or average number of cigarettes smoked per day.
Results: Participants in the active condition significantly reduced CO levels from baseline (M = 10.18 ppm) to end of treatment (M = 5.80 ppm; $t(29) = 3.26$, $p = .004$) and at a six week post-treatment follow-up (M = 6.59 ppm; $t(26) = 4.27$, $p < .001$). Comparatively, participants in the control condition did not significantly reduce CO from baseline (M = 10.85 ppm) to end of treatment (M = 9.20 ppm; $t(31) = 1.92$, $p = .067$) but did at a six week post-treatment follow-up (M = 7.61 ppm; $t(30) = 3.71$, $p = .001$). Urinary cotinine data were correlated with average CO levels (r's = .50 range), and the pattern of cotinine data across conditions was similar to that of CO levels.
Conclusions: These findings indicate this Internet-based CM program should be feasible for use with rural adolescent smokers and may circumvent many of the logistical barriers in applying CM treatments to younger smokers in rural regions.
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OPIATE USE AND OUTPATIENT DRUG TREATMENT ARE ASSOCIATED WITH LACK OF TRUST IN POINT-OF-CARE RAPID TESTS.

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Aims: Drug treatment programs are important HIV testing venues for high-risk individuals. Recent advances in point-of-care rapid testing for HIV, hepatitis B, C and syphilis highlight the potential of drug treatment programs for expanding their role beyond HIV testing into sexually transmitted infections testing. Hypothesis: We hypothesized that a sub-sample of drug users would express mistrust of point-of-care rapid testing. The data for the current study come from a randomized controlled trial of non-FDA approved point-of-care rapid tests for HIV, hepatitis B and C, and syphilis.
Methods: This analysis focused on men and women who are current participants in the randomized trial (N = 689). Procedures: All participants gave informed consent using a form approved by the California State University, Long Beach, Institutional Review Board; provided blood specimens for rapid and gold standard tests for HIV, hepatitis, and syphilis; and completed questionnaires to assess the testing experience. Participants were asked whether they endorsed the statement "I trust the accuracy of rapid test results." Statistical Analysis: All associations were assessed using logistic regression.
Results: The sample was 55% male, 39% Black, 27% White, 24% Latino, 10% reported Other as their ethnicity, and the mean age was 40.4 years (SD = 12.1). Results: Factors positively associated with trusting rapid test results were having had a previous rapid test [OR=7.90, 95% CI 1.16, 53.47] and being homeless [OR=7.88, 95% CI 1.25, 49.49]; factors negatively associated with trusting rapid test results included outpatient drug treatment [OR=.14, 95% CI .02, .90], number of days used other opiates in past month [OR=.88, 95% CI .80, .98] and number of days used alcohol in past month [OR=.90, 95% CI .84, .97].
Conclusions: Educational interventions should be part of testing efforts in outpatient drug treatment facilities especially as a greater variety of point-of-care rapid tests receive FDA approval.
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LIABILITY FOR RISK BEHAVIORS: RACIAL DIFFERENCES.

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Aims: Two measures of risk for developing substance use disorders (SUD), the Transmissible Liability Index (TLI) and the Non-transmissible Liability Index (NTLI) have been developed and validated in previous work by the authors. The current analysis extends this work to examine whether TLI and NTLI scores at age 10-12 predict a range of risky behaviors at age 19, and to determine if the accuracy of the predictions differ between European-Americans (EA) and African-Americans (AA).
Methods: Subjects were N=478 boys (N= 373 EA, N= 105 AA) enrolled in the CEDAR prospective study of drug abuse in families when they were 10-12 years old. Risk behaviors measured at age 19 included self-reported criminal acts, nicotine dependence, behavioral dysfunction, social skills, job performance, family adjustment, antisocial personality (ASP) symptoms, and number of sexual partners in the past 3 years. Statistical analyses consisted of bivariate predictions using linear or logistic regression.
Results: TLI scores predict self-reported criminality, nicotine dependence, behavioral dysfunction, social skills, job performance, family adjustment, ASP symptoms and number sexual partners. In racial group comparisons, TLI scores predicted outcomes better in EA for criminal acts, ASP symptoms, nicotine dependence, family adjustment, leisure and recreation, social skills, job performance and number of sex partners. In contrast, NTLI scores predicted outcomes better in AA for behavior problems, family adjustment, and number of sex partners.
Conclusions: Results suggest that in EA, transmissible risk better forecasts risky behavior than in AA. In contrast, nontransmissible risk better forecasts such behavior in AA. Many areas of research on genetic and transmissible risk for SUD have relied largely on EA samples; these findings may not generalize to AA who may be underserved in applied settings and in research. Moreover, AA may be exposed to a greater level of environmental risk such that transmissible risk factors may play lesser etiological roles in the development of chronic behavior problems.
Financial Support: P50 DA005605
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STRAIN DIFFERENCES IN MEASURES OF BEHAVIORAL-REGULATION RELATED TO DRUG ABUSE IN RATS.

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Aims: A fundamental challenge for any complex nervous system is to regulate behavior in response to a variety of environmental challenges. Genetic polymorphisms give rise to different predispositions in how a given organisms responds to environmental challenges, some of which are maladaptive. For example, individual differences in sensation seeking, attention, and impulsivity have been associated with risk for developing drug abuse. We examined behavioral-regulation in response to environmental challenges designed to measure sensation seeking, attention and impulsivity which have been associated with drug abuse in eight inbred rat strains to determine the genetic heritability.
Methods: Locomotor response to novelty (LRN), sensory reinforcement (SR), choice reaction time (CRT), and delay discounting (DD) were tested in 8 inbred strains of rats (n=9 for each strain) (Male August Copenhagen Irish, Brown Norway, Buffalo, Fischer, Lewis, Spontaneous hypertensive rat (SHR), Wistar Kyoto (WKY), Dahl salt sensitive (SS)). LRN and SR have been hypothesized to be animal models of human sensation seeking and have been linked to drug abuse. The speed and variability of responding on the CRT tasks has been hypothesized to reflect ADHD related attention deficits. Premature responding on CRT tasks have been hypothesized to reflect the "action impulsivity" and has been linked to drug abuse. DD measures the degree to which delay decreases reward value and has been hypothesized to be a measure of "choice impulsivity" and has been linked with drug abuse.
Results: There were large strain differences on all of the tasks with strain differences accounting for between 0.66 and 0.43 of the total variance.
Conclusions: These results indicate that genes have substantial influence on complex behavioral phenotypes related to drug abuse and provide the basis for future studies aimed at more precisely determining genotypes and the interaction of these genotypes with environmental influences.
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A LONGITUDINAL STUDY OF ORGANIZATIONAL FACTORS AND IMPLEMENTATION OF MEDICATION-ASSISTED TREATMENTS FOR ADDICTION.

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Aims: Despite a wealth of evidence supporting the use of Medication Assisted Treatment (MAT) for substance use disorders, uptake and sustained use of this evidence-based practice (EBP) remains weak. Research indicates that adoption of EBPs is associated with organizational or environmental factors, characteristics of the individuals, and the implementation process. Identification of the specific factors which impact use of MAT may facilitate access to this innovative treatment.
Methods: This longitudinal study examined organizational and provider factors impacting use of MAT over a ten-year period. Survey data was collected in three waves and included face-to-face interviews with program administrators from a national sample of privately funded treatment programs (n=171). A generalized estimating equations (GEE) negative binomial regression model was used to examine the number of SUD medications prescribed by private programs over the study period.
Results: Results indicate that staff and organizational factors including administrator education level, accreditation status, and having a physician on staff were positively associated with the number of SUD medications prescribed over time. Programs with a greater percentage of revenues from private insurance prescribed more SUD medications, while programs with a higher percentage of referrals from the criminal justice system prescribed fewer SUD medications.
Conclusions: Our findings indicate that access to MAT increased over the ten-year study period in the sample of privately funded-treatment programs. Results also indicate that specific organizational factors continues to play a critical role in successful adoption of medication in SUD treatment. Efforts to enhance access to MAT for patients with SUDs may require interventions that address provider and organizational capacities and preparation.
Financial Support: This work was supported by the NIDA, Award K23DA021225 and NIDA Grant R01DA13110

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PREDICTING ADOLESCENT MARIJUANA USE: THE ROLE OF SCHOOL SUPPORT AND POSITIVE MARIJUANA EXPECTANCIES.

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Aims: Marijuana use continues to be a problem among adolescents. There has been increasing empirical attention to the influence of school environments on the development of marijuana use—particularly with regard to the early onset of use. Much of this work has focused on threats in the school environment with limited attention to supportive school climates that potentially deter substance use as well as mechanisms through which school environments are associated with use. The current longitudinal study examined the role of positive marijuana use expectancies as a mediator of the relation between school support and marijuana use.
Methods: We examined self-reported school support, marijuana expectancies, and marijuana use in a sample of 246 youths (girls = 46%) annually over three years. At the first wave of data collection participants' ages ranged from 11 – 15 (mean = 13, SD = .81); 53% of the sample was White, 38% African American, and 9% "Other." We tested a model in which school support predicted changes in positive marijuana expectancies, which, in turn, predicted changes in past-year marijuana use over three years.
Results: The model fit the data well: $\chi 2$= 1.386, CFI = 0.99, TLI = 0.97 and RMSEA = 0.04 (90% CI = 0.00 – 0.19). There was a marginally significant indirect effect of school support at year 3 on past-year marijuana use at year 5, via positive marijuana expectancies at year 4, controlling for all prior waves of marijuana expectancies and use (Est = -0.04, SE = 0.02, p = 0.07).
Conclusions: These findings highlight the importance of enhancing specific environmental factors—such as school support—in intervention efforts to reduce substance use among adolescents. Results are discussed within a social disorganization theory framework.
Financial Support: NIDA Grant R01 DA018647-08

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BEYOND SEXUAL PARTNER CONCURRENCY: OVERLAPPING INJECTION PARTNERSHIPS AMONG HIGH-RISK COUPLES IN NORTHERN MEXICO.

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Aims: Concurrent (overlapping) sexual partnerships potentiate HIV transmission by increasing sexual network connectivity, but concurrency methodology has rarely been applied to injection drug use. We sought to assess concurrent syringe sharing among injector dyads, which we hypothesized would be associated with injection duration/frequency, stimulant use, and sex risk behaviors.
Methods: We selected injection drug users (IDUs) from a cohort of female sex workers and their intimate partners in Tijuana (TJ) and Ciudad Juárez (CJ), Mexico. Surveys measured demographic, relationship, and drug/sex risk profiles. Descriptive regression analyses assessed recent syringe sharing within/outside of dyads and identified independent correlates of concurrent syringe sharing within and outside of dyads during the same period.
Results: All 200 IDUs (100 dyads) injected heroin, and 42% also used illicit stimulants (methamphetamine, cocaine, crack). In the past six months, 75 IDUs (38%) shared syringes with partners, 73 (37%) shared with others, and 28 (14%; 16 women, 12 men) shared concurrently with partners and others. Residing in CJ, higher depression scores and injecting heroin multiple times per day (vs. less often) were independently associated with increased probability of concurrent syringe sharing. Among men, using stimulants and having concurrent sex partners were also positively associated with concurrent syringe sharing.
Conclusions: Overlapping injection partnerships involving syringe sharing may be associated with addiction severity and sexual risk. Since concurrent syringe sharing with intimate partners and others could increase HIV transmission throughout IDUs' networks, qualitative and social network studies are needed to identify ways to reduce sharing behaviors.
Financial Support: This work was supported by the National Institute on Drug Abuse grant numbers R01DA027772, R36DA032376, T32DA023356 and K01-DA026307; and the National Institute of Allergy and Infectious Diseases grant number T32-AI007384.

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INCREASING PREOPERATIVE SLEEP REDUCES POSTOPERATIVE PAIN AND ANALGESIC USE.

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Aims: Suboptimal management of postoperative pain increases the risk of chronic pain and opiate abuse. Given the bidirectional relation of sleep and pain, we hypothesized that post operative pain and analgesic use could be reduced in joint replacement "short sleepers" who increased bedtime pre operatively vs those remaining on their habitual sleep schedule.
Methods: Twelve patients, 3 men, 9 women, 50.3+/-12.5 yrs old, who were scheduled for joint replacement (6 knee and 6 hip) and reported < 7 hrs nightly sleep participated. Seven were randomized to a nightly extension (1-2 hrs) of their habitual bedtime (EXT: 4 knee, 3 hip) and five remained on their habitual (HAB: 2 knee, 3 hip) schedule during the week before surgery. They were monitored by actigraphy. The outcome measures were the postoperative daily dose of opiates (converted to morphine mg equivalents) and the daily pain ratings (5-6 times daily on a 0-10 scale: 0= no pain and 10=worst pain experienced) over the 1-3 day in-hospital recovery.
Results: On a one week sleep diary before the preoperative week those in the EXT group reported 6.8 (0.4) hrs and the HAB group 6.6 (0.9) hrs of time in bed nightly. During the one week preoperative sleep manipulation, compared to the HAB group the EXT group spent significantly more time in bed nightly (8.0 vs 6.9 hrs, $p<0.03$), which resulted in significantly more sleep time (6.8 vs 5.8 hrs, $p<0.04$). On the 1-3 day postoperative in-patient recovery the EXT group reported significantly less daily pain (4.2 vs 5.5, $p<0.01$) than the HAB group, despite a trend ($p<0.06$) for less daily morphine mg intake (25.2 vs 46.5 mg).
Conclusions: These data demonstrate prophylactic preoperative improvement of sleep reduces post operative pain and opiate use. It demonstrates the analgesic potential for preoperative sleep extension and consolidation in patients with other sleep disorders.
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TRAINING UNDERGRADUATE STUDENTS IN ADDICTION-RELATED TOPICS USING IN-PERSON AND ONLINE INSTRUCTIONAL FORMATS: IMPLICATIONS FOR PREPARING THE BEHAVIORAL HEALTH WORKFORCE.

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Aims: Health Reform implementation will help drive integration of physical and behavioral health. It is essential to expose allied health students to addiction-related education early in their academic careers significant since studies have shown that nurses, social workers, physicians, healthcare workers, and psychologists report feeling unprepared to intervene with patients with SUDs. Currently, there are 345 universities/colleges with addiction programs with most courses taught in-person. In 2011 over a third of all college students reported taking an online academic course. Existing data demonstrate the efficacy of online courses. However, limited data exist comparing the effectiveness of in-person vs. online instruction for addiction-related courses. This study compared the effectiveness and student satisfaction of in-person vs. online undergraduate generalist addiction courses.
Methods: An in-person introductory undergraduate generalist addiction course at the University of Nevada Reno was originally developed in 1998. Course faculty later developed an online version ensuring that course content, assignments, and testing/grading methods/criteria were equivalent. Both courses are offered during each semester.
Results: During the Spring 2011 through Fall 2012 semesters, the in-person course was completed by 762 students; 435 completed the online version of the course. The total average satisfaction and usefulness scores were 4.47 and 4.35 respectively for the in-person course, and 4.45 and 4.65 for the online course (5-point Likert scale). Complete item analysis will be presented.
Conclusions: To adequately prepare the behavioral health workforce for health reform, access to undergraduate addiction courses must be expanded. Based on this study, expansion may be achieved by offering equivalent online and in-person addiction courses as student ratings were high for both instructional formats.
Financial Support: Funded by SAMHSA/CSAT: Mountain West and Pacific Southwest ATTCs

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THE EFFECTS OF MENTHOL CIGARETTE USE ON TREATMENT OUTCOMES IN AN INTERVENTION FOR WEIGHT-CONCERNED SMOKERS.

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Aims: Several studies have shown that individuals who smoke menthol cigarettes are less likely to quit smoking and more likely to relapse during a quit attempt. The current study investigated menthol cigarette use as a potential moderator of smoking cessation outcomes in a predominately white sample of treatment-seeking smokers.
Methods: This is a secondary analysis of data from a randomized controlled trial of low-dose naltrexone augmentation of nicotine replacement designed to examine smoking cessation and post-cessation weight gain in weight-concerned smokers (Toll et al., 2010).
Results: In the primary study, seven-day point-prevalence smoking abstinence rates at 26 weeks post-quit date were not significantly different between the 2 groups (naltrexone: 22% vs. placebo: 27%, $p = 0.43$). However, analyses revealed that menthol use predicted quit success. Among menthol smokers ($N = 61$), 13% were abstinent at Week 26, and among non-menthol smokers ($N = 105$), 30% were abstinent (Wald = 6.02, $p = .01$; OR, 2.90; 95% CI, 1.24-6.81). Further, menthol smokers who quit smoking gained significantly more weight at Week 26 ($M = 14.87$ lbs., $SD = 9.08$; $t(37) = -2.22$, $p = .03$) than non-menthol smokers who quit ($M = 7.95$ lbs., $SD = 7.53$).
Conclusions: Menthol cigarette use has not typically been evaluated as a mechanism for differences in smoking cessation outcomes, but emerging evidence suggests that use of menthol cigarettes may make smoking cessation more difficult. This study adds to the literature supporting the claim that smoking menthol cigarettes can have adverse effects on smoking cessation efforts and on other cessation-related outcomes, such as post-cessation weight gain.
Financial Support: Research supported by NIH grants T32-DA007238 (AMR) and P50-AA15632 (SOM).

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MEASUREMENT OF DRUG-LIKING IN ABUSE POTENTIAL STUDIES: A COMPARISON OF BIPOLAR VS. UNIPOLAR VISUAL ANALOG SCALES.

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Aims: Measures of drug-liking used in abuse potential studies are typically quantified on 100-mm visual analog scales (VAS) that can be either unipolar (liking measured using the entire scale) or bipolar (liking and disliking measured with the midpoint considered neutral). The present analysis examined the relationship between these two rating scales in an abuse potential study of oxycodone.
Methods: A single-center, randomized, double-blind, placebo-controlled, crossover study was conducted in two cohorts of healthy volunteers with a history of recreational drug abuse. Following a naloxone challenge and drug discrimination test, participants received one treatment per day; cohort 1: 40mg oxycodone, 40mg crushed OxyContin®, 40mg or 80mg OxyContin®, or placebo; cohort 2: 20, 40, or 80mg oxycodone or placebo. As part of the abuse potential assessment, the Drug Effects Questionnaire (includes: Do you like the drug?) and bimodal drug-liking scale (Do you like the drug effect you are feeling now?) were administered at multiple post-dose intervals. Spearman correlation coefficients were calculated for individual VAS scores, Emax (highest post-dose score) and TEmax (time to Emax) combined and separately for each cohort and treatment.
Results: 35 male, non-dependent, recreational drug users participated. Among all values (n=2477), there was a positive correlation between bipolar and unipolar ratings (r=0.64). A higher correlation (r=0.85) was observed for Emax values and a weaker correlation (r=0.23) for TEmax. Similar correlations were observed for each cohort. Among treatments within each cohort, individual score correlations were higher for oxycodone (0.44 to 0.74) than placebo (-0.16 and 0.09).
Conclusions: These data suggest a reasonable positive correlation between unipolar vs. bipolar VAS ratings of drug-liking, especially for Emax. Data interpretation is limited by the use of one study drug and the systematic ordering of questions.
Financial Support: Analysis was sponsored by Pfizer Inc.

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NO ASSOCIATION BETWEEN CRACK-COCAINE DEPENDENCE AND FUNCTIONAL INTRONIC POLYMORPHISM AT DOPAMINE D2 RECEPTOR GENE.

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Aims: DRD2 gene is commonly expressed in two distinct isoforms, the short and the long variant, due to alternative splicing. The change G>T (rs2283265), located in intron 5, influences the splicing, where the T allele favors the long form. The aim of this study was to verify if this DRD2 polymorphism is associated with CCD, since T allele has already been associated with cocaine abuse.
Methods: A cross-sectional sample of 237 current adult crack abusers or dependents (DSM-IV TR criteria) from in- and outpatient clinics and 210 community non-crack-cocaine users (controls) were collected in southern Brazil. Subjects were evaluated with ASRS, ASI6 and MINI-Short. IQ was estimated using WAIS. DNA samples extracted from whole blood were genotyped for the DRD2 rs2283265. The hypothesis of association was investigated using Chi-square.
Results: The G allele and the GG genotype were the most prevalent in both cases (80.2% e 62.9%, respectively) and controls (80.3% e 63%, respectively). A paired analysis comparing the frequencies for G and T alleles showed no differences between cases and controls (Mcnemar p=0.56; 189 pairs regarding sex, age and ethnic group). The non-paired analyzes including all the 447 subjects also did not show differences (Pearson Chi-square p=0.98). The comparison of GG, GT and TT genotype frequencies between cases and controls did not evidenced associations in both paired (Mcnemar p=0.60) and non-paired (Pearson Chi-square p=0.99) analyses.
Conclusions: This study suggests that DRD2 gene, namely intron 5 G>T change, is not associated with CCD. However, in our population, this polymorphism has been recently implicated in alcohol dependence when interacting to the dopamine D4 receptor gene (DRD4). Thus, further analyses including DRD4 gene might be able to reveal a role for DRD2 gene in CCD.
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ARE PERSONALITY DISORDERS OR ADHD LINKED TO COCAINE-INDUCED PSYCHOSIS IN COCAINE-DEPENDENT PATIENTS?

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Aims: Cocaine induced psychosis (CIP) is common but not present in all cases.A lifetime diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), Antisocial Personality Disorder (ASPD) and Borderline Personality Disorder (BPD) has been proposed to be associated with the CIP. However, the evidence for these associations is proving to be controversial. Aims:To study the presence of CIP in a large sample of cocaine-dependent patients (615, 78.5% men; 35.5(18-69 yo), SD 8.04) and to determine the relationship between ASPD,BPD or ADHD and CIP.
Methods: A structured interview about psychotic symptoms and drug dependence was systematically conducted with 586 of the patients. The SCID-II and CAADID-II were used to identify ASPD, BPD or ADHD comorbidity. Finally, we included 314 patients in the study(80.3% men; 35.7(20-63 yo),SD=7.93). We conducted a descriptive analysis and then we used Chi Square to study qualitative variables.
Results: CIP were detected in 59.8% of the sample studied. We identified a significant association between CIP and both adult ADHD (X2= 10.84,p=.001) and ASPD(X2= 5.30,p=.022). We failed to identify association between CIP and BPD(X2= 2.11,p=.145). However, we discovered an association between history of cannabis-dependence and CIP(X2= 7.30,p=.007).
Conclusions: We hole that CIP is related to ASPD, ADHD and cannabis-dependence lifetime comorbidity in cocaine-dependent patients. These findings can also be useful for a clinical approach and to avoid the risk of a psychotic state in cocaine-dependent patients.
Financial Support: We are grateful for the Grant of the Departament de Salut. Government of Catalonia. Spain for studding cocaine dependence.
We are grateful for the Grant FIS EC07/90713 of the Instituto Carlos III, of the Spanish Government "Eficacia de la cafeína en el mantenimiento de la dependencia de la cocaína".

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SUGAR DEPENDENCE: ASSOCIATION WITH PSYCHIATRIC DISORDERS, GENDER AND OBESITY.

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Aims: The theoretical construct of added sugar dependence has recently been investigated, and a number of studies address issues related to the excessive intake of sweets and the possible association with abuse and dependence. The aim of this study was to verify the association between added sugar dependence and other co morbidities.
Methods: A sample of 1,081 individuals (47% female, mean age 35±12yrs) responded to a questionnaire on added sugar dependence based on DSM-IV criteria and another on other psychoactive substances dependence (MINI-Plus), the Fagerström test for nicotine dependence, the Barratt Impulsiveness Scale (Bis-11) and the Binge Eating Scale (BES. Data were collected in two Brazilian state capitals. Analyses included Chi Square and binary logistic regression.
Results: Overall, 39% of the sample had a diagnosis of substance dependence (10% marijuana, 14% cocaine, 25% alcohol and 29% nicotine) and 25% of added sugar dependence; 35% were obese and 13% had eating disorders (9% moderate and 4% severe). After bivariate analyses, subjects with substance dependence had more added sugar dependence than non-substance dependence (31% vs. 20%; p<0.001); obese had more added sugar dependence than non-obese (35% vs. 23%; p<0.006); presence of eating disorders had more added sugar dependence than those who had not eating disorders (66% vs. 19%; p<0.001). Subjects with higher levels of impulsivity had more added sugar dependence than those with lower levels (34% vs. 17%; p<0.001). The strongest correlates of added sugar dependence were female gender (OR=3.5, 95% CI=2.4-4.9), substance dependence (OR=2.8, 95% CI=1.9-4.0), obesity (OR=1.9, 95% CI=1.3-2.9) and high impulsivity (OR=1.9, 95% CI=1.4-2.6).
Conclusions: Results suggest an association between added sugar dependence and substance dependence, impulsivity, obesity and gender. Added sugar dependence is a plausible hypothesis, since sugar seems to share pathways with the cerebral reward system.
Financial Support: CNPq; FAPEMIG

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NON-OPIOID SUBSTANCE USE AMONG OPIOID-DEPENDENT PATIENTS ENROLLING IN OPIOID TREATMENT PROGRAMS: A LATENT CLASS ANALYSIS.

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Aims: To determine whether distinct classes of enrollees into opioid treatment programs (OTPs) can be classified based on their non-opioid substance use.
Methods: Self-report data on past 30 day illicit substance use (opioids, alcohol, non-opioid prescription and illegal drugs) and sociodemographics were collected from a nationwide sample of 7,979 enrollees into OTPs (primarily methadone maintenance). Latent class analysis (LCA) was used to classify subjects based on their non-opioid substance use and multinomial logistic regression was used to predict these substance use groups based on type of opioid drugs used and other characteristics (demographics, pain, treatment history).
Results: The most frequently used non-opioid drugs were cannabis (40%), anti-anxiety medications (34%) and cocaine (25%). LCA identified a 5-class (C) model. C1 (58.7%), had low risk of using non-opioid drugs. C2 (23.5%) had high risk of using anti-anxiety drugs and moderate risk of cannabis. C3 (8.8%) had high risk of using non-opioid prescription drugs (anti-anxiety, sleep, and muscle relaxant drugs) and cannabis. C4 (6.2%) had high risk of using marijuana and cocaine. C5 (2.8%) had high risk of using all non-opioid drugs. Compared to C1 (the low-using group), participants in the other classes were younger, female, tobacco users, had chronic pain, inject opioids, and used both prescription opioids and heroin. The two non-opioid prescription drug groups (C2, C3) were more likely to report chronic pain and use prescription opioids. C4 (marijuana/cocaine users) and C5 (polydrug users) were more likely to report injection.
Conclusions: Aggregation of substance use may obscure important subgroup differences in patterns of illicit non-opioid drug use. The identification of two groups that primarily misuse prescription drugs and that have comparatively high rates of chronic pain suggests that self-medication may play a role among sub-groups of OTP patients.
Financial Support: Denver Health is part of the Researched Abuse Diversion and Addiction-Related Surveillance(RADARS®)System.

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BRIEF HIV ASSESSMENT FOR SCREENING CJ OFFENDERS IN ADDICTION TREATMENT.

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Aims: Efficient data collection in high-volume offender drug-using populations has increased demand for assessments that offer diagnostic screening of selective needs. The present study provides psychometric information on a one-page, self-report instrument of 19 items known as the TCU HVHP Form designed to provide information on HIV and hepatitis risks associated with injection drug use, sexual activities, attitudes toward condom use, and health concerns about HIV. In addition, we provide data on the predictive validity of HIV measures completed as part of a Disease Risk Reduction intervention (WaySafe).
Methods: Offenders from eight prison-based treatment programs for substance abuse were assessed at intake (N=1055). The primary instrument was the TCU HVHP along with several background assessments including motivation, psychological functioning, social functioning, and criminal thinking. The TCU WaySafe intervention assessment (administered prior to offenders exiting treatment) included five composite measures: HIV Knowledge Confidence, Avoiding Risky Sex, Avoiding Risky Drug Use, HIV Testing Awareness, and Risk Reduction Skills.
Results: Principal components analysis of the HVHP form identified four scales: Injection Risk Behavior, Condom Risk, Sex Risk Behavior, and AIDS Concerns with coefficient alpha reliabilities ranging from .72 to .87. Predictive validities of the scales were demonstrated by their correlations with measures of the WaySafe intervention. The injection risk scale was significantly and negatively correlated with the avoiding risky drug use WaySafe measure. Correspondingly, the condom risk scale was significantly correlated with the avoiding risky sex WaySafe measure. The HVHP scales had significant correlations with measures of psychological functioning including risk taking, hostility, depression, anxiety, self-esteem and decision making.
Conclusions: Findings support use of this brief screening tool to help identify treatment needs in correctional settings.
Financial Support: Funding was provided by NIDA / NIH through a grant to TCU R01DA025885.

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A MICRODIALYSIS AND BEHAVIOURAL INVESTIGATION OF MODAFINIL IN FREELY MOVING RATS.

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Aims: Modafinil is a stimulant used to treat narcolepsy. Its pharmacology is enigmatic, but reports suggest modafinil is a dopamine reuptake inhibitor in human brain in vivo (Volkow et al, 2009, JAMA;301:1148).
Methods: The Culex Bambino automatically collects samples from dual microdialysis probes and simultaneously measures locomotor activity in freely-moving rats. The effects of modafinil (100, 300 and 600mg/kg po) on extracellular levels of noradrenaline (NA), dopamine (DA) and 5-HT in prefrontal cortex (PFC) and striatum (STR) and locomotor activity were determined ≤5hr post-dosing.
Results: No significant ($p<0.05$) neurochemical or behavioural changes were produced by modafinil (100mg/kg po). In PFC, modafinil (300 & 600mg/kg) produced moderate increases in the efflux of DA (≤214%) and NA (≤263%). The onset of DA efflux was more rapid and peaked earlier (30min) than NA (105 120min). In STR, modafinil produced small increases of extracellular DA (≤137%) that were rapid in onset and peaked at 60min. It had no effect on 5-HT efflux in PFC or STR. Modafinil (300 & 600mg/kg po) dose-dependently enhanced locomotor activity. At the lower dose, rats were active for ~2hr, whereas at the higher dose they were active throughout the 5hr experiment. No correlation existed between the increase in STR DA efflux after modafinil (600mg/kg po) and the degree of locomotor activation ($r2 = 0.002$; $p = 0.857$).
Conclusions: These data reveal that modafinil enhances neurotransmission by NA and DA in PFC and DA in STR. The effects were small in comparison to d amphetamine or methylphenidate. Modafinil substantially increased locomotor activity. The lack of correlation between STR DA efflux and locomotor activity suggests other neurotransmitters have a role in modafinil's behavioural effects.
Financial Support: Shire Pharmaceutical Development Ltd

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ESTIMATING CAPACITY REQUIREMENTS FOR SUBSTANCE USE TREATMENT SYSTEMS: POPULATION-BASED APPROACH.

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Aims: Development of a needs-based planning model for substance use services and supports across Canada that aligns with the estimated needs of the populations of local health regions and yields estimates of required treatment capacities along the continuum of care.
Methods: 1. Estimate the number of people in need of substance use treatment, by problem severity, within a given year by using population survey data.
2. Estimate the probable help-seeking population based on a synthesis of the literature.
3. Estimate the optimal trajectory of cases across several defined categories of treatment services, including SBIRT, to yield the number of people to plan for in each service setting.
4. Conduct a gap analysis between the estimated capacity and the current capacity of substance use services at five pilot sites across Canada.
Results: The model development process and gap analyses at the five pilot sites yielded fairly consistent results. Results indicate that withdrawal management services appear to be over-supplied in many regions. The current supply of low-threshold community services such as brief treatment closely reflect the model's estimates; however, gaps appear to exist for more intensive community services such as day treatment. Significant gaps also appear to exist for residential services across Canada. Gap analysis results were corroborated by staff at the pilot sites. Results also indicate the need for more systematic SBIRT processes to engage clients in the treatment system.
Conclusions: The model appears to have face value when applied to Canada as a whole; however, regional context should be taken into account when applying the model to local jurisdictions. We anticipate that the model will serve as a valuable tool for substance use treatment system planners to use in discussions and decisions about funding and resource allocation. Next steps include model adjustments using more precise regional data and incorporating the model into a larger needs assessment process.
Financial Support: Health Canada's Drug Treatment Funding Program, Project no. 6559-15-2009/10350002

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VITAL SIGNS: A NATIONAL STUDY OF THE ADDICTION TREATMENT PROFESSION.

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Aims: To describe the characteristics of the substance abuse treatment workforce and common strategies to prepare, retain and maintain the workforce.
Methods: The ATTC Network conducted a national survey of clinical directors at substance abuse treatment facilities via a 57 item instrument available in online and paper format. A simple random sample of treatment facilities was drawn from I-SATS using an a priori power analysis. Nationally, an 88% response rate was achieved with an N of 491.
Results: Clinical directors are primarily white (86%), women (59%) over 50 (60%), well educated (57% Master's) and licensed or certified (86%). Direct care staff members are also primarily white (64%) and women (67%), but are generally younger than clinical directors with 75% aged younger than 54 years. Direct care staff members are educated (36% Master's; 24% Bachelor's) and are either already licensed/certified (54%) or are pursuing licensure/ certification (18%).
Clinical directors reported a past-year direct care staff turnover rate of 18.5%. Almost half of respondents (49%) reported that their treatment facility had difficulty filling open positions, for reasons such as lack of qualified applicants (63%) and insufficient funding (43%). Also, 68% of respondents experience barriers to providing staff training and professional development.
Conclusions: These results have significant implications for the future of the addiction treatment workforce. Most notably, these findings suggest that the workforce is aging and lacking in diversity with substance abuse treatment agencies finding it difficult to recruit and retain qualified professionals.
Financial Support: This study was completed by the ATTC Network under a cooperative agreement from SAMHSA

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NEW YORK'S CENTER FOR EXCELLENCE IN INTEGRATED CARE: THE SYSTEM IS SHOWING SIGNIFICANT IMPROVEMENT.

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Aims: Since November 2008, the Center for Excellence in Integrated Care (CEIC) has been assessing and providing technical assistance to New York State substance abuse and mental health outpatient programs. This is a statewide effort to improve the ability of these outpatient clinics to deliver integrated substance abuse and mental health services in the areas of Screening, Assessment, and Evidence-based Interventions to persons with co-occurring conditions. CEIC fosters improved and integrated services through on-site, "hands on" technical assistance.
Methods: Using the Dual Diagnosis Capability in Addiction [or in Mental Health] Treatment (DDCA[MH]T), CEIC has evaluated 546 addiction or mental health programs to date, generating an analysis of the system's capability to provide integrated services.
Results: These evaluations revealed a system average of 2.70 (on a 5-point scale), which indicates a level closer to Dual Disorder Capable (DDC) than to basic (Addiction or Mental Health Only Services) and that there is a need for further improvement to achieve a "capable" (DDC) status. Follow-up on a sample of 117 clinics to date indicates a significant improvement in capability from 2.69 at Time 1 to 3.03 at Time 2, with significant increases shown in all seven dimensions of the measurement instrument. The number of programs at a capable level doubled from 26% to 52% 12-15 months after time 1. In addition, the study demonstrated a significant relationship between the DDCAT score and time-in-treatment, often seen as a proxy for good client outcomes.
Conclusions: The study demonstrates the capacity to use a measurement and a technical assistance process to bring about system-wide change. The results indicated that the system is showing significant improvement. The methods and approaches employed have the potential to foster the further integration of substance abuse, mental health, and primary care, an essential process for health care reform.
Financial Support: New York State Health Foundation awards 2008-2496857, 2009-3426912, & 11-20788

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SCREENING AND BRIEF INTERVENTION FOR DRUG USE IN PRIMARY CARE: THE ASPIRE RANDOMIZED TRIAL.

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Aims: The efficacy of universal screening and brief intervention (SBI) for drug use among primary care (PC) patients is unknown; consequently it is not recommended by professional organizations. This 3-arm study tested the efficacy of two brief interventions (BIs) for drug use—a brief negotiated interview (BNI), and an adaptation of motivational interviewing (AMI)—compared to no BI in PC patients identified by screening.
Methods: We randomly assigned subjects identified by screening with the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) drug specific scores of ≥4 to: BNI, AMI or no BI. BNI was a 10-15 minute structured interview conducted by trained paraprofessional health educators. AMI was ≤45 minutes of MI and an optional booster conducted by trained doctoral psychology students. Primary outcome was number of days use of self-identified drug of most concern (DOMC) in the past 30 as determined by validated calendar method at 6 months. Analyses were performed using negative binomial regression adjusted for baseline use, drug dependence, DOMC, and prior outpatient counseling.
Results: Of 876 eligible subjects, 528 (60%) were randomized. Subjects were: mean age 41, 70% male, 69% black. DOMC was: marijuana 63%, opioid 17% (prescription opioid 11%), cocaine 19%. ASSIST score was ≥27 (consistent with dependence) for 18%; 12% reported injection drug use (past 3 months); mean days DOMC use (of 30) was 14.4; at 6 months it was 14.0. At 6 months, 98% completed follow-up. Mean *adjusted* days use of DOMC at 6 months was 11.5 (no BI) vs. 11.2 (BNI)(incidence rate ratio (IRR) 0.97, 95% CI 0.77-1.22) and 12.1 (AMI)(IRR 1.05, 95% CI 0.84-1.32)(p=0.81 for both comparisons vs. no BI). There were no significant effects of BNI or AMI in analyses stratified by DOMC or ASSIST score.
Conclusions: BI does not appear to have efficacy for decreasing drug use in primary care patients identified by screening. Future analyses will examine 6-week outcomes and additional 6-month outcomes including hair drug tests.
Financial Support: R01-DA025068, UL1-TR000157

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ADOLESCENT PATIENTS IN SUBSTANCE ABUSE TREATMENT: EXAMINING CALLOUS-UNEMOTIONAL TRAITS.

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Aims: Callous-unemotional (CU) traits are measurable in childhood, stable across time and predict poor outcomes. Accordingly, developers of the DSM-V have proposed a CU-trait specifier for conduct disorder. Relatively little work has examined this newly proposed categorical measure of CU-traits, especially in clinical populations.
Methods: Adolescent patients in substance abuse treatment (n=147) completed diagnostic assessments and measures of CU traits. Among patients with Conduct Disorder (CD) (n=111) we sought: to test the prevalence of the CU-trait specifier; to compare groups with and without CU traits for differences in demographics, estimated IQ, prevalence of mental health diagnoses, and severity of CU on dimensional measures; and, to examine the sensitivity and specificity of the CU-trait specifier against high levels of CU from dimensional measures.
Results: About half (49%) of CD patients met the proposed criteria for the CU-trait specifier. CD patients with CU traits, compared to those without, were about one-third as likely to have had attention-deficit/hyperactivity disorder (ADHD), predominantly hyperactive-impulsive type in their lifetime and were significantly less likely to have had an alcohol use disorder. On average, patients with CU traits, compared to patients without, scored significantly higher on dimensional measures of CU ($p<0.01$); however, examination of individual data suggested that some youths not meeting the CU-trait specifier scored highly on dimensional measures of CU; the opposite was also true.
Conclusions: The proposed CU-trait specifier is common among adolescents in substance abuse treatment. Against expectations, the CU-trait specifier did not identify a group of patients with more severe externalizing behavior problems.
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POST-RETRIEVAL PROPRANOLOL MAY ALTER RECONSOLIDATION OF TRAUMA MEMORY IN INDIVIDUALS WITH PTSD AND COMORBID ALCOHOL DEPENDENCE.

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Aims: We recently completed a laboratory study of a novel medication intervention that targeted attenuation of trauma related distress by altering trauma memory reconsolidation in individuals with PTSD and comorbid alcohol dependence (AD). The medication intervention consisted of the administration of the β-blocking agent, propranolol, immediately following the presentation trauma cues (the cues initiate the reconsolidation). A placebo control group was also employed. In a test session performed the next day, we examined subjective distress and alcohol craving to both trauma and alcohol cues. It was hypothesized that propranolol-treated PTSD+AD individuals would evidence lower distress and craving during the test session than placebo-treated individuals.
Methods: PTSD+AD participants received either 40 mg propranolol (n=21) or placebo (n=23) immediately after trauma cue exposure (description of participant's worst trauma presented via headphones). After remaining overnight in an alcohol-free environment, participants received a 'test' session of cue exposure that was identical to the first session except (a) trauma cue exposure was followed by alcohol cue exposure, and (b) no medication was administered. Subjective distress and craving were measured (100 point scale) prior to, during, and following cue exposure in both sessions.
Results: Compared to placebo-treated participants (M= 56.0, se= 3.7), propranolol-treated (M= 42.8, se= 4.0) participants evidenced significantly lower distress to the combined trauma-alcohol cues presented during the test session (p= .03). The groups did not evidence any difference in craving.
Conclusions: This study provides the first evidence that propranolol administration following trauma cue exposure may modulate trauma memories in PTSD+AD humans. Implications for basic neuroscience and drug addiction treatment will be noted.
Financial Support: NIAAA grant 5RC1AA019019 (M. E. Saladin, PI), USPHS grant M01 RR01070 & NIH Grant Numbers UL1 RR029882 and UL1 TR000062.

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THE RELATIONSHIP BETWEEN POSTPARTUM DEPRESSION AND CHANGE IN PERINATAL ALCOHOL USE: AN ANALYSIS OF PRAMS DATA.

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Aims: Postpartum depression (PPD) is common and more likely to affect women with drug and alcohol problems. Although most women quit drinking during pregnancy, approximately 10% continues. This study investigated the relationship between postpartum depression and change in perinatal alcohol use.
Methods: The study population was from the Pregnancy Risk Assessment Monitoring System, 2004-8 births which is a population-based surveillance and collects data from postpartum women on health behaviors before, during, and shortly after pregnancy. Women who self-reported any alcohol use during the 3 months before pregnancy were included in analysis. Overall change in alcohol use (difference between self-reported use in 3 months before and last 3 months of pregnancy) was compared between those with and without PPD. Also, change in heavy (7 or more drinks/week) and binge drinking (5 or more drinks/sitting) by PPD status were examined. Bivariate analysis and logistic regression were performed using the weight functions.
Results: The study sample consisted of 64,595 women of whom 10% reported PPD. Most women (87%) quit drinking during pregnancy, although 1.4% and 0.4% reported binge and heavy drinking, respectively, in the last 3 months of pregnancy. PPD was more common among women who continued drinking compared to who quit or reduced use (AOR 1.30[95% CI: 1.07, 1.55]). Moreover, any binge drinking during pregnancy was associated with PPD (AOR 1.53 [95%CI: 1.06, 2.20]), whereas heavy drinking was not (AOR 0.90 [95% CI: 0.43, 1.88]).
Conclusions: These findings suggest several associations between postpartum depression and change in perinatal alcohol use, highlighting the need for vigorous screening and treatment for both PPD and alcohol use in this population.
Financial Support: None

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PRECLINICAL INVESTIGATION OF THE ABUSED SYNTHETIC CANNABINOID CP47,497.

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Aims: CP47,497 and other synthetic cannabinoid compounds were incipiently synthesized as research tools to investigate mechanisms by which marijuana affects the brain and for the development of potential therapeutic drugs. Over the past few years, these compounds have resurfaced on the designer drug market. The goal of this research was to characterize the behavioral effects of CP47,497 using well-established preclinical in vivo models, tetrad and drug discrimination, to evaluate cannabimimetic effects. Complementary pharmacological and genetic approaches will be used to determine whether CB1 receptors mediate the pharmacological effects of CP47,497.
Methods: ICR mice (n=8) were tested in the tetrad paradigm that assesses catalepsy, antinociception, hypothermia, and decreases in spontaneous locomotor activity. In drug discrimination experiments, C57BL/6J (n=8-12) mice were trained to discriminate 5.6 mg/kg THC from vehicle.
Results: CP47,497 was significantly more potent than THC in each parameter of the tetrad and in drug discrimination studies. The CB1 receptor antagonist, rimonabant, blocked all effects of CP47,497 but required high doses (10 mg/kg) to antagonize the antinociceptive, hypothermic and locomotor depressant effects. In accordance with these data, all cannabimimetic effects of CP47,497 were abolished in CB1 (-/-) mice. Furthermore, in drug discrimination studies, CP47,497 fully substituted for THC; demonstrating a potency 5 times that of THC.
Conclusions: Collectively, these results indicate that acute administration of CP47,497 elicits markedly more potent effects (i.e. 5-7 fold) when compared to THC. Since these products are almost exclusively smoked, ongoing research is investigating inhalation exposure of CP47,497, to further address the pharmacology and bioavailability of this abused synthetic cannabinoid.
Financial Support: Research supported by NIDA F31DA033183 (KLS), P01DA009789 (AHL), T32DA007027 (WLD).

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TIME OF ABSTINENCE PRIOR ADMISSION TO A RESIDENTIAL REHABILITATION PROGRAM AS A PREDICTOR OF COCAINE DEPENDENCE TREATMENT COMPLETION IN LIMA, PERU.

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Aims: Cocaine dependence is a prevalent condition among the Hispanic population. In Peru, cocaine is the first psychoactive substance for which people seek treatment in rehabilitation programs. Treatment retention is a well known predictor of treatment outcomes. Approximately 50% of patients drop out of rehabilitation programs. Research focusing on factors that may increase treatment retention rates could have an important impact on treatment results. The aim of this study is to estimate if time of abstinence prior to admission to a residential rehabilitation program might increase treatment completion rates in cocaine dependent individuals.
Methods: Data are from patients that were admitted into the residential treatment program of "Centro de Rehabilitacion de Ñaña", a governmental treatment center in Lima, Perú, between years 2002 – 2009 (n= 644 males, age 18+ years). A logistic regression model was used to estimate the magnitude and significance of association between patients discharge status (treatment compliance and dropout) and weeks of abstinence prior treatment in cocaine dependent individuals, with a null hypothesis of no difference in treatment discharge status.
Results: Subjects with more than three weeks of abstinence had higher treatment completion rates as compared to subjects with three weeks of abstinence or less, with and without statistical adjustment for covariates (e.g., age, cocaine route of administration) at $p<0.01$.
Conclusions: In this preliminary cross-sectional study, the evidence suggests that having more than three abstinence weeks prior to admission into the rehabilitation program could predict higher completion rates. Further studies are needed to confirm these finding and explore its implications in treatment policy.
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IMPACT OF GROUP MOTIVATIONAL INTERVIEWING (GMI) ON DUALLY DIAGNOSED VETERANS WITH ALCOHOL USE DISORDERS.

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Aims: Despite promising results in a prior study showing that GMI resulted in enhanced treatment engagement and reduced substance use compared to standard treatment (ST) among dually diagnosed inpatients who went to any treatment and continued to use substances (Santa Ana et al., 2007), MI in a group format remains under-investigated. The aim of the current study was to conduct a second RCT evaluating the efficacy of GMI relative to ST for lowering substance use among dually diagnosed veterans in a substance abuse outpatient program (SATC).
Methods: Veterans (n = 118) with current alcohol dependence/abuse and a co-existing DSM-IV-TR Axis I disorder were randomized to GMI or ST through the Charleston, SC VAMC SATC. Patients attended four 1-hour sessions of GMI or ST across 4 days. GMI sessions were consistent with the spirit of MI with the goal of eliciting change talk. ST sessions consisted of standardized educational presentations on addiction. Data analyses used analysis of covariance with zero inflated negative binomial distribution. Standard errors were corrected for group level nesting.Using the Time Line Follow Back (Sobell & Sobell,1992), we measured daily and peak alcohol consumption (in standard ethanol content units; SECs) at 3-month follow up.
Results: Participants in GMI relative to ST consumed less alcohol in SECs (b = -155.3 (70.9), t = -2.19, p = .03) and drank fewer standard drinks in terms of their peak (highest) drinking day (b = -4.78 (2.03), t = -2.4,p = .02). No baseline differences between groups were found on alcohol consumption. This report is a preliminary analysis of a larger RCT evaluating the impact of GMI on treatment engagement, substance use, and change talk.
Conclusions: MI can be used in a group format for lowering alcohol consumption among veterans with alcohol use disorders in a substance abuse outpatient setting and may be a useful intervention that is easily added to existing treatment.
Financial Support: This study was funded by a VA Clinical Science Research & Development (CSR&D) career development award to PI: Elizabeth J. Santa Ana (CDA-2-016-08S).

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DSM-5 CRITERIA FOR GAMBLING DISORDERS AND ITS EFFECTS ON THE ASSOCIATION WITH OTHER PSYCHIATRIC DISORDERS.

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Aims: The DSM-5 will likely remove the "illegal acts" criterion from the definition of pathological gambling (PG). We investigated if such a change would have an impact on the prevalence of PG, and on the types of psychiatric disorders associated with PG. We compared PG prevalence rates using DSM-IV and DSM-5 criteria, and examined the association of common psychiatric disorders, including impulsivity traits [Antisocial Personality Disorder (ASPD) and Paranoid Personality Disorder (PPD)], Major Depression Disorder (MDD) and Obsessive/Compulsive Disorder (OCD), with PG, using the two alternative DSM definitions of PG.
Methods: Data came from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2. After exploratory analyses, weighted logistic regressions were used to examine if lifetime psychiatric disorders were associated with past year/lifetime PG. Analyses were stratified by gender and were adjusted by age, ethnic group and household income.
Results: Lifetime PG prevalence was lower using the DSM-IV vs. DSM-5 criteria both in women (0.20% vs. 0.33%) and men (0.59% vs. 0.93%), although the difference was not significant. A considerable proportion of cases of PG (31.12%-DSM-IV and 39.62%-DSM-5, respectively) did not meet criteria for other common psychiatric disorders. In men, ASPD (OR= 5.33[1.80-15.78] vs. OR = 3.72[1.36-10.21], using DSM-IV vs. DSM-5 criteria) and PPD (OR = 3.80[1.27-11.41] vs. OR =4.23[1.45-12.29]) were associated with past year PG irrespective of the DSM criteria followed. In contrast, in women, MDD and OCD were associated with PG using DSM-5 criteria (OR=4.53[1.87-10.97] vs. OR=3.10[1.35-7.11], respectively), and only MDD was associated with PG using DSM-IV criteria (OR=3.45[1.06-11.22]).
Conclusions: The prevalence of PG, as well as its associations with common psychiatric disorders, varies by the type of selected DSM criteria. Males and females exhibit different pathways into the development of gambling addiction, suggesting the need for gender-specific prevention responses.
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CORRELATES OF LIFETIME CIGARETTE USE AND DEPENDENCE BY MID-ADULTHOOD IN A NON-WESTERN (MAURITIAN) SAMPLE.

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Aims: This study examined correlates of lifetime cigarette use and dependence in Mauritius, a small island country in the Indian Ocean with people primarily of African or Indian heritage. Based on findings in other sub-Saharan African countries and India, we hypothesized being male, less educated, and having lower occupational status would be associated with increased likelihood of lifetime smoking and more severe nicotine dependence. Given religious proscriptions for substance use, we expected Muslims to have the lowest rate of smoking, followed by Hindus and Tamils, and then Creoles. We expected that Muslims and Hindus who viewed their religion as important would be less likely to be smokers.
Methods: Participants were 1,170 of the original 1,795 participants of the Joint Child Health Project, a birth cohort study that has followed participants since 1972 when they were 3 years old. Nicotine dependence severity when participants were in their mid to late 30s.
Results: Fourty-six percent of men and 4% of women were lifetime smokers. Creole women (17%) were more likely to be smokers than women in other ethnic groups (0-3%). Creole men (57%) were more likely than Hindu men (39%) to be lifetime smokers, with about half (49%) of Tamil and Muslim men being smokers. Within men, lower education, lower occupational status, and being Creole were associated with lifetime smoking. Hindu, Tamil, and Creole men had similar patterns of correlates, but education and occupation were not associated with smoking in Muslims. None of the independent variables were associated with dependence severity.
Conclusions: Results are consistent with previous findings of high rates of smoking in African and Indian men, but also indicate relatively high rates of smoking among Creole women. Our findings suggest socioeconomic variables may be differentially associated with smoking across ethnic groups.
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PATHWAYS OF PROGRESSION FROM ONE SUBSTANCE USE TO ANOTHER IN TREATMENT SEEKERS.

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Aims: Patients usually start from licit and less harmful substances before progressing on to more severe substances of use. The aim was to assess the pattern of progression from one substance use to another in a consecutive sample of substance users attending the outpatient of de-addiction service in north India.
Methods: Patients attending the de-addiction services of Post Graduate Institute of Medical Education and Research, a tertiary care hospital in North India were recruited. All newly registered patients with any substance use disorder. Information about demographic details and substance use pattern was gathered using a structured questionnaire.
Results: Four hundred and six consecutive participants were enrolled. Most of the subjects were male, married, employed and of urban background. Of the total number of patients, 273 (67.2%) were dependent on more than one substance. In this sample of more than one substance dependence, the substance of first dependence in descending order of frequency was tobacco (83.9% of cases), opioids (28.9%), alcohol (18.3%), cannabis (7.0%) and sedatives (2.6%).
Conclusions: In this particular centre, opioids were being reported as the first drug of dependence in a considerable proportion of cases. Knowing about the types of substances to which patients become dependent upon has public health implication. Preventive measures can be streamlined focusing on the drugs on which patients get dependent first. Educational and therapeutic strategies can be utilized to halt progression to other substances.
Financial Support: Non funded project

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AN EXPLORATION OF CHILDHOOD EXPERIENCES AMONG A SAMPLE OF HOMELESS VETERANS.

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Aims: This secondary analysis was conducted to examine childhood experiences among a sample of homeless veterans with co-occurring mental health and substance use disorders enrolled in the SAMHSA-funded MISSION treatment study.
Methods: A sample of 406 veterans completed a comprehensive intake assessment which included the SCID, ASI, BASIS 32, and GPRA questionnaires. Additionally, a childhood-related risk factor measure was administered to categorize the experiences of veterans during childhood according to mental health/substance use diagnosis, legal status, and housing experiences while growing up.
Results: The majority of respondents were male (95%), African American (61%), between the ages of 45-55 (51%), and served during the post-Vietnam service era (62%). Many veterans reported physical violence in the home during childhood (34%). Almost a quarter of the sample reported at least one parent having mental health issues (23%) and near daily alcohol (62%) or drug use (35%) by a member of the household. Among respondents, 28% received public assistance while 18% lived in public housing. The majority of veterans also reported getting suspended, expelled, or dropping out of school (63%).
Conclusions: This analysis of childhood experiences provides additional information needed to better understand the varied experiences of homeless veterans with co-occurring disorders. Clinicians and researchers should take into consideration the childhood experiences of homeless veterans in order to better address the underlying issues that might affect housing, legal, mental health, and substance abuse outcomes as an adult. The current findings may hold important clinical implications for the VA's goal of ending veteran homelessness by 2015.
Financial Support: SAMHSA-CSAT Grant # TI16576

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ROLE OF α3GABA$_A$ RECEPTOR MODULATION IN THE ANTI-CONFLICT EFFECTS OF BENZODIAZEPINE-TYPE DRUGS IN MONKEYS.

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Aims: Benzodiazepines (BZs) are abused widely, yet it is not clear to what extent abuse-related effects can be dissociated from therapeutic effects such as anxiolysis. Recent data have suggested that α3 subunit-containing GABA$_A$ receptors (α3GABA$_A$ receptors) may play a role in the abuse-related effects of BZs. Here, we evaluated the role of this receptor subtype in anxiolytic-like effects.
Methods: Rhesus macaques (n=3) were trained on a multiple component operant conflict procedure. A fixed ratio (FR) 18 was in effect for food (non-suppressed responding, NSR) while in alternating components a concurrent FR20 for a mild noxious stimulus (suppressed responding, SR) was in effect. Anxiolytic-like effects were concluded by increases in responding during the SR components. A range of doses of 3 novel α3GABA$_A$ functionally-selective compounds were administered i.v.: EMJ-I-026 (0.3-10 mg/kg), YT-III-31(0.1-1 mg/kg), and YT-III-271(0.03-3 mg/kg).
Results: EMJ-I-026 produced significant rate-suppressant effects in the NSR component ($F(4,7)=4.32$; $p=0.045$) at 10 mg/kg with no significant increase in SR rates, although 1 animal showed full anxiolytic-like effects at 1 and 3 mg/kg. YT-III-31 showed a trend towards increasing SR ($F(3,6) = 3.664$; $p = 0.08$) at 1 mg/kg, but also reduced NSR rates in 2 of 3 monkeys. YT-III-271 had no significant group effects, but increased SR rates in 1 monkey.
Conclusions: These results suggest that, in contrast to abuse potential, the α3GABA$_A$ receptor may not play a key role in BZ-induced anxiolysis, since compounds acting at this receptor do not exhibit robust anti-conflict effects separable from rate-decreasing effects.
Financial Support: These studies were supported by DA011792, DA033795, MH046851, the Lynde and Harry Bradley Foundation, Research Growth Initiative UWM, and RR000168/OD011103.

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CHILDHOOD ABUSE IS ASSOCIATED WITH ALCOHOL USE OUTCOMES AFTER GENDER RESPONSIVE TREATMENT FOR WOMEN IN PRISON.

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Aims: Previous research has shown beneficial outcomes of gender-responsive vs. standard substance abuse treatment for women in prison. This secondary analysis associates days of alcohol use with randomization into trauma-focused, gender-responsive substance abuse treatment (GRT), experience of childhood abuse (physical/sexual; CA), and the interaction between GRT and CA. It was hypothesized that GRT and CA would interact to yield differential alcohol use outcomes in the 12-month period following treatment.
Methods: From 04/2006-11/2008, 115 incarcerated women were randomized into GRT (n=55) or standard prison-based treatment (n=60). Assessments occurred at intake, 6-, and 12-months. The hypothesis was tested with longitudinal negative binomial regression, controlling for age, race, education, marital status, years of alcohol abuse at intake, and time between assessments.
Results: Most participants were white (48%) or Latino (26%), had at least a HS/GED equivalent (65%), and were married/previously married (57%). Three participants did not disclose childhood abuse history. Multivariate analysis (n=112) showed that childhood abuse and randomization into gender-responsive treatment produced no significant direct effects on alcohol use, however, the interaction effect showed that women reporting CA who were randomized into GRT revealed significantly reduced rates of alcohol use (IRR=0.38; 95% CI=0.16-0.88).
Conclusions: Incarcerated women reporting CA evidenced superior alcohol use outcomes after GRT, demonstrating that the trauma-focused intervention was more effective when participants had themselves experienced prior trauma. Findings support the application of GRT in populations of women with high rates of prior trauma/abuse.
Financial Support: This study was funded by NIDA (Grant R21 DAO18699-01A1), an Interagency Agreement (Contract 07-002467) between UC Davis and UCLA and a NIDA NRSA fellowship (Grant T32DA07272-20).

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SELF-REPORTED COLLISION INVOLVEMENT ASSOCIATED WITH DRIVING AFTER ALCOHOL USE, CANNABIS USE OR BOTH.

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Aims: Research suggests that driving under the influence of alcohol (DUIA) and driving under the influence of cannabis (DUIC) increases the risk of collision involvement. It has been suggested that the increased collision risk associated with DUIC may in fact be attributable to alcohol, since it is often used together with cannabis. We examined self-reported collision involvement associated with DUIA, DUIC or both in the past 12 months.
Methods: Data were derived from the CAMH Monitor, an ongoing population survey of Ontario adults (18 years and older). Data from 2002 to 2010 were merged for this study (N=16,054). Analysis examined self-reported collision involvement in the past 12 months by four groups (no DUIA and no DUIC, DUIA only, DUIC only, or both DUIA and DUIC).
Results: We found significant differences in the prevalence of self-reported collision involvement by driving after substance use. Drivers reporting neither DUIA nor DUIC had the lowest prevalence of collision involvement (6.7%), those reporting either DUIA or DUIC alone reported higher prevalence of collision involvement (8.6% and 13.8% respectively). Nearly a third (30.5%) of drivers reporting both DUIA and DUIC reported collision involvement.
Conclusions: These results suggest that any increase in collision risk associated with DUIC cannot simply be attributed to alcohol. Individuals who report both DUIA and DUIC in the past year report a very high prevalence of collision involvement. More research is needed to determine the reasons for this finding.
Financial Support: Funding was provided by AUTO21, a member of the Networks of Centres of Excellence program that is administered and funded by the Natural Sciences and Engineering Research Council, Canadian Institutes of Health Research, and Social Sciences and Humanities Research Council, in partnership with Industry Canada.

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EFFECTS OF WORKING-MEMORY TRAINING IN METHADONE MAINTENANCE PATIENTS.

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Aims: Working memory (WM) is the capacity to store and manipulate small amounts of information to serve current goals; it is often impaired in methadone maintenance patients (MMP). With executive function as its core component, WM is critical for overall cognitive functioning. The purpose of this randomized controlled trial with MMP was to test the effects of a cognitive training program that has been shown to improve WM and other cognitive functions in other populations.
Methods: MMP were randomly assigned to an experimental group who performed 25 sessions of computerized WM training (TRAIN) or an active control group who performed a version of the program that does not train WM (CON). An assessment battery measuring WM, other cognitive functions, and substance use treatment outcomes was administered before and after training.
Results: Preliminary analyses on WM outcome measures were conducted in 45 MMP (22 female). The TRAIN (N = 23) and CON (N = 22) groups did not differ on age, gender, level of education, estimated IQ, or methadone dose (ps > 0.35). Within the TRAIN group, improvement on the WM training tasks themselves was comparable to improvement observed in other clinical populations undergoing similar training. Within-group t-tests indicated that the TRAIN group showed significant improvement ($p < 0.05$) from pre- to post-training on both a verbal WM task (WAIS Digit Span Backwards) and a visual-spatial WM task. The CON group did not show improvement on these tasks. Additional analyses will be conducted to test the effects of training on other cognitive functions and substance use treatment outcomes.
Conclusions: These preliminary results suggest that WM is malleable in response to training in MMP and that improvement on WM training tasks can transfer to non-trained WM tasks. As WM is a core cognitive process that is necessary for the performance of many cognitive functions and that may support recovery from substance use disorders (e.g., treatment engagement, substance use avoidance), this finding has potentially important clinical implications.
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TRANYLCYPROMINE ENHANCES PROPENSITY TO ACQUIRE SELF-ADMINISTRATION OF A LOW DOSE OF NICOTINE.

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Aims: Nicotine (NIC) reduction has been suggested as a potential regulatory tool to lower the abuse liability of cigarettes. However, the effects of NIC in the context of other pharmacologically active constituents and biochemical effects of tobacco smoke must first be understood. The present study sought to determine whether the acquisition of self-administration of a low dose of NIC could be affected by differences in two types of non-NIC conditions, (1) MAO inhibition, and (2) a cocktail of tobacco constituents thought to contribute to reinforcement: acetylaldehyde, harman, norharman, anabasine, anatabine, cotinine, myosmine, and nornicotine.
Methods: Adult male Sprague Dawley rats were allowed to nosepoke on a fixed ratio 2 for infusions of a solution containing a low dose of NIC (10 μg/kg/infusion) and one of three dose levels of cocktail: standard cocktail (constituent levels proportionally matched to those in cigarettes given a standard self-administration dose of nicotine), 10-times-standard cocktail (all standard constituent concentrations multiplied by 10), or without cocktail. Rats were injected intraperitoneally with either MAO inhibitor tranylcypromine (TCP) (1 mg/kg) or saline 1 hour before each of 16 daily self-administration sessions, each 1-hour long (N=16-18 for each of the 6 subgroups in the 2-by-3 design).
Results: Pre-session TCP administration caused a greater proportion of rats to acquire self-administration, (80% vs. 45% in no TCP groups, $p<.001$). TCP resulted in a faster increase in infusions over the 16 sessions and a higher stable infusion rate relative to no TCP ($p<.001$), and this distinction maintained when rats that did not reach a criterion of self-administration were excluded. However, cocktail dose did not have a significant effect on acquisition.
Conclusions: Cumulatively, these findings show that TCP increases the likelihood that rats will acquire NIC self-administration and results in significantly more infusions being earned for rats that do acquire, perhaps through MAO inhibition.
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THE ASSOCIATION BETWEEN EXECUTIVE FUNCTION, RISKY INJECTION PRACTICES AND HEPATITIS C VIRUS AMONG INJECTION DRUG USERS.

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Aims: To measure associations between impaired executive functioning (e.g., planning and problem solving ability) as measured by the Tower of London (TOL) and outcomes of risky injection practices, and Hepatitis C virus (HCV) among injection drug users (IDU).
Methods: Data from the Neuro-HIV Epidemiologic Study, a study of neurobehavioral risk factors and infectious disease among injection and non-injection drug users in Baltimore, was restricted to those who had ever injected in their lifetime (n=458). Impaired executive function was defined as a TOL standardized total excess moves score below the 10th percentile. Injection practices were dichotomized and included ever having shared needles, cookers, cotton, rinse water and ever having backloaded in one's lifetime. The outcome of HCV was binary. Logistic regression was performed to assess the association between impairment on the TOL and each of the risky injection behaviors and HCV infection. Mediation analyses were conducted to assess the extent to which the association between TOL and HCV were attenuated by the hypothesized injection intermediates.
Results: Impairment on the TOL was associated with greater odds of ever having shared a cooker (OR: 1.99, 95% CI: 1.16-3.44), or cotton (OR: 1.92, 95% CI: 1.15- 3.22), and ever having backloaded (OR: 1.69, 95% CI: 1.00- 2.83). Impaired individuals had 1.97 (95% CI: 1.05- 3.73) times the odds of HCV infection compared to intact individuals. Mediation analyses suggested that the association between TOL and HCV was mediated by risky injection practices.
Conclusion: Interventions designed to reduce infectious disease among IDU should aim to improve planning and problem solving abilities to reduce risky injection practices.
Conclusions: Interventions designed to reduce infectious disease among IDU should aim to improve planning and problem solving abilities to reduce risky injection practices.
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MARIJUANA AS A PREDICTOR OF CONCURRENT SUBSTANCE USE AMONG MOTOR VEHICLE OPERATORS.

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Aims: Previous literature has discussed the high rates of cocaine, opioid and benzodiazepine use among users of marijuana, however, no research has addressed the rates of concurrent use among drivers. This is of particular concern as each of these substances may produce effects which are detrimental to driving safety, and the concurrent use of these substances may compound this effect. The current study is one of the first attempts to examine the role marijuana has on polysubstance use among drivers.
Methods: The current research examines rates of marijuana abuse and dependence among an active sample of drivers (N = 7,734) pulled from the 2007 National Roadside Survey (NRS). The NRS was designed to estimate the prevalence of substance use among a random national sample drivers. Mean age of participants was 36.89, and the majority of the sample was White (59.2%) and male (60.1%). Participants provided self-report items, oral fluid and blood samples.
Results: Participants who used marijuana but did not meet diagnostic criteria for Abuse (n = 165) or Dependence (n = 112) were significantly more likely to test positive for THC, cocaine, opioids, and benzodiazepines than were those who did not use marijuana. Further, those that met criteria for Marijuana Abuse and Dependence were more likely than those who used marijuana but did not meet criteria to test positive for THC, cocaine and benzodiazepines and THC, cocaine, and opioids respectively.
Conclusions: As marijuana gains ever more popularity and its legal status is revisited, understanding how it may impact driving is vital. The current study demonstrates that drivers who meet diagnostic criteria for Marijuana Abuse or Dependence were more likely to test positively for other substances.The current study provides valuable information on the need for services to address marijuana use and concurrent substance use.
Financial Support: The NRS was funded by the NHTSA (DTNH22-6-C-00040) and by the NIAAA (R01 AA0016407). Analysis and reporting were supported by grants R01 AA0016407, R01 AA018352, P20 AA017831 and NIDA T32DA007292.

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REVIEW OF HUMAN ABUSE POTENTIAL STUDY METHODOLOGY FOR ABUSE-DETERRENT FORMULATIONS.

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Aims: Abuse/misuse of prescription drugs is a significant problem. Various novel approaches to mitigate such use incorporate abuse- and tamper-deterrent features into higher risk products, eg, opioids. Such products should be evaluated in humans prior to marketing to determine their abuse potential. Methodological issues with these products differ from those of new chemical entities and specific design considerations are needed.
To provide review of methodology for clinical evaluation of ADFs.
Methods: ADF approaches may include chemical or physical barriers, prodrugs or agonist/antagonist combinations. Many products aim to deter intranasal (IN) and/or intravenous (IV) use; some products may also deter oral abuse. Abuse potential studies must consider the physicochemical and pharmacological nature of the investigational product (IP), and clinical studies assessing the intended/unintended routes of administration (ROA) should be performed when safe or feasible. Subjects should be experienced recreational drug users, and should also have experience with tampering and/or the relevant ROA. Single doses of IP and comparator are generally used, as the effects of the drug substance are usually well-understood. Multiple doses of the IP and comparator may be needed for some products, eg, those providing "overdose protection". Studies should typically include placebo. One challenge is the manipulation of products, eg, crushing for IN/IV use. Manipulations and administration must be carefully standardized. In addition, due to obvious (intended) differences in formulations, blinding may present a challenge and must be balanced against the need to evaluate the "real-world" nature of the product. A reduced battery of traditional study endpoints may be used, ie, those most relevant to abuse and class of interest. Finally, standard statistical analysis is used and may incorporate a "responder" analysis.
Conclusions: Traditional human abuse potential study design can be applied to the evaluation of ADFs; however, design modifications may be needed.
Financial Support: INC Research Toronto Inc and Pfizer Inc.

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RCT OF DRUG COUNSELING AND ABSTINENCE CONTINGENT BUPRENORPHINE IN MALAYSIA.

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Aims: To evaluate whether the efficacy of office-based buprenorphine maintenance treatment (BMT) with brief physician management (PM) and weekly medication dispensing in Malaysia is improved by provision of weekly, individual behavioral drug and HIV risk reduction counseling (BDRC), abstinence-contingent provision of take-home doses of buprenorphine (ACB), or the combination of BDRC and ACB.
Methods: Opioid-dependent individuals completing BMT induction (N=234) were randomly assigned to 26-weeks of BMT+PM, BMT+PM+BDRC, BMT+PM+ACB, or BMT+PM+BDRC+ACB. PM was provided by 2 primary care physicians working in busy private practice clinics. BDRC was provided by specially trained nurses. Primary outcomes were proportions opioid-negative urine tests and proportions meeting criteria for protective transfer for persistent illicit opioid use.
Results: Patients were all male; mean (SD) age 38.7 (10.5) years; 95% ethnic Malay; 93% less than high school education; 44% employed full time; 25% married; 38% current ATS use; 9% HIV positive; 70% Hepatitis C positive. There were no significant baseline differences among treatment conditions. Retention averaged 145 (51) days out of 182 of offered active treatment and did not differ significantly among groups. Proportions of opioid-negative tests across randomization cells were 50% for PM only, 57% for PM+BDRC, 62% for PM+ACB, and 75% for PM+BDRC+ACB ($p<0.001$); differences related to both treatment components were also statistically significant (ACB: $p<0.002$, BDRC: $p<0.05$). 25 patients met criteria for protective transfer: 14 assigned to PM only, 4 to PM+BDRC, 5 to PM+ACB, and 2 to PM+BDRC+ACB ($p<0.002$).
Conclusions: The study results support the feasibility and the efficacy of providing behavioral counseling (BDRC), simple contingency management using take-home medications to reinforce abstinence (ACB), and the combination of BDRC+ACB during office-based BMT in busy primary care practices in Malaysia.
Financial Support: R01 DA014718; K24 DA00445; CMHC/DMHAS/State of Connecticut

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A RANDOMIZED TRIAL OF A COMPUTERIZED BRIEF INTERVENTION FOR DRUG USE IN PRIMARY CARE: 3-MONTH OUTCOMES.

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Aims: To examine baseline characteristics and 3-month outcomes of adult primary care patients enrolled in a randomized trial comparing computerized brief intervention (CBI) v. interpersonal brief intervention (IBI).
Methods: Patients seen in two federally qualified health centers (FQHCs) in rural New Mexico were recruited and screened with the WHO Alcohol, Smoking, and Substance Involvement Screening Tool (ASSIST). Patients with moderate-risk drug use (ASSIST score between 4 and 26) were eligible for participation. The IBI was delivered by experienced behavioral health counselors and based on motivational interviewing. The CBI was designed to mirror the content of the IBI. General linear mixed model approach will be used to examine changes in ASSIST scores from baseline to 3-month follow-up for the CBI and IBI conditions.
Results: 2,048 patients completed eligibility screening with the ASSIST, of whom 65.5% scored in the low-risk category for illicit drug use, 28.1% in the moderate-risk category, and 6.4% in the high-risk category. 360 moderate-risk participants enrolled in the randomized trial, with 182 randomized to the CBI and 178 to the IBI condition. Participants were 90% white, 46.9% Hispanic, and 46.1% female. Mean age of the sample was 36.0 years (SD=14.7). Past 3-month marijuana use was reported by 87.2% of the sample, while 18.6% used cocaine, 16.7% used sedatives, 11.4% used methamphetamine, and 20.3% used opioids. Polydrug use was reported by 36.4%. Mean baseline global continuum of illicit substance involvement score on the ASSIST was 19.0 (SD=14.5). Changes in ASSIST scores from baseline to 3-month follow-up for the CBI and IBI conditions will be presented.
Conclusions: A substantial number of moderate-risk drug-using patients eligible for a brief intervention were identified at two rural FQHCs. Differences between conditions will be discussed.
Financial Support: Funded through NIDA 1R01DA026003 (PI Schwartz)

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IMPULSIVITY IN SUBSTANCE DEPENDENCE: A META-ANALYSIS.

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Aims: To quantitatively summarize studies that applied standardized questionnaires to assess impulsivity in individuals diagnosed with substance dependence, including cocaine, heroin, alcohol, cannabis, and tobacco dependence. Impulsivity has been implicated as a factor related closely to substance dependence. So far no meta-analysis has been conducted to quantitatively summarize results from these studies.
Methods: We used the keywords "impulsivity" and "dependence" to narrow down our search on Medline and Science Direct to include all studies that had reported impulsivity scores using validated and reliable questionnaire. Behavioral testing results will be analyzed separately. We searched all English language studies from 1990 to August 2012. A total of 52 reports met the inclusion criteria and were reviewed by three abstractors independently. We had further narrow down the number to generate weighted mean differences from pooled data using RevManager 5.0 from Cochrane analysis.
Results: We included 4 papers on substance dependence in general, 4 on alcohol dependence, 5 on cocaine dependence, 1 on heroin dependence, 1 on cannabis dependence, 1 on nicotine dependence and 2 on polysubstance dependence. The most commonly used instrument was the Barratt Impulsivity Scale, although the UPPS impulsive behavior scale and the Dickman Impulsivity Inventory were also used, specifically in more recent studies. Results indicate high impulsivity scores compared to normal controls across all domains, especially in cognitive and non-planning impulsiveness. Impulsivity was also directly related to aggression and self harm and inversely to age of onset. Results indicate that impulsivity remains stable throughout the period of substance use and treatment. Limits of questionnaire results and key differences to behavioral assessments will be discussed
Conclusions: Impulsivity is significantly higher in substance dependents than controls. Motor impulsivity and non-planning impulsivity are key domains, which result in higher impulsivity scores. Treatment implications are discussed.
Financial Support: Supported by funding from PHSA (Province of British Columbia, Canada)

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NUMERATORS AND DENOMINATORS TO QUANTIFY THE ABUSE OF PRESCRIPTION OPIOIDS: A REVIEW OF DATA SOURCES AND METRICS.

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Aims: The recent increase in therapeutic use of prescription opioids for pain management has been associated with increased diversion and nonmedical use of these products, an emergent public health concern particularly in the U.S. There are no universally adopted standardized metrics for measuring the estimated prevalence of abuse, or abuse relative to drug utilization, i.e. an "abuse ratio." This methodological review will address the relative strengths and limitations of the various numerators and denominators that can make up an abuse ratio, the utility of the ratio itself, and data sources available for the ascertainment of these metrics.
Conclusions: Crude numbers (numerators) associated with outcomes of substance abuse (i.e. hospitalizations, emergency room visits, detox or inpatient treatment admissions, overdoses) cannot be properly understood without context. A denominator is critically important in providing that context by accounting for opioid exposure availability or populations at risk of exposure. The impetus for selecting appropriate numerators and denominators is the construction of a prescription opioid abuse ratio to estimate the prevalence and incidence of abuse among those directly exposed, to estimate abuse relative to drug dispensed, and to compare abuse for various opioid drugs. Interpretation of this ratio is dependent on the denominator selected to define exposure availability. Abuse ratios in the literature are observably disparate in the inclusion of specific metrics, and there is no consensus in the field regarding which numerators and denominators allow for the most appropriate approximation and comparison of the extent of prescription opioid abuse. Although certain metrics are preferable for a given abuse ratio, each comes with caveats that must be explained upfront.
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HANDLING AND VEHICLE INJECTIONS IMPACT CORTICOSTERONE BUT NOT ADRENOCORTICOTROPIC HORMONE LEVELS IN SPRAGUE-DAWLEY BUT NOT LEWIS RATS.

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Aims: The hypothalamic–pituitary–adrenal (HPA) axis is a key factor in the addiction trajectory. HPA hormones levels change in response to standard experimental procedures, yet few studies have compared such changes in Lewis and Sprague-Dawley (SD) rats, two strains commonly used in rodent models of addiction. In this study, HPA activity in these two strains was compared after different handling and injection schedules, to explore the extent that HPA responses differ by strain and individual differences underlie addiction vulnerability.
Methods: Adult male Lewis (n=32) and SD rats (n=32) were exposed to one of four treatments (n=8/group): no handling (NH), short or long handling (SH/LH), and saline injections (SI). In SH/LH groups, rats were handled 3x/day at 1hr intervals and sacrificed after 7 days (SH) or 14 days (LH) of handling. SI rats received saline injections 3x/day at 1hr intervals, mimicking a binge-like pattern of cocaine exposure. After the last handling bout or injection, rats were anesthetized with CO2 and decapitated. Plasma levels of adrenocorticotropic hormone (ACTH) and corticosterone (CORT) were measured using radioimmunoassay.
Results: All rats gained weight during the study. While the weights of LH/SH rats did not differ by strain, SD rats gained more weight than did Lewis rats during saline injections ($P<0.01$). Across all treatments, ACTH levels were consistently higher in SD than Lewis rats ($P<0.01$). There was an interaction between treatment and strain on CORT levels ($P<0.01$); CORT levels were elevated after NH and SH only in SD rats ($P<0.05$). ACTH and CORT levels varied across SD individuals. Strain differences in CORT levels reduced in magnitude with extended handling and neutral injections.
Conclusions: Findings point to potential mechanisms underlying strain differences in self-administration studies and emphasize the importance of extended handling prior to experimenter-administered drug exposures.
Financial Support: NIH-NIDA P60DA05130 (MJK), F32DA030831 (KSC)

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USING TINCTURE OF OPIUM FOR TREATMENT OF OPIATE ABUSERS IN IRAN.

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Aims: Iran has implemented nationwide opiate substitution programs delivered through a network of more than 3,000 private and governmental treatment centers. Since 2011, tincture of opium (TO) has been introduced to the network as well. Domestic research had shown the safety and effectiveness of such agonist in special group of clients (e.g. opium smokers and the elderly). In the current research effectiveness of TO substitution and very gradual tapering in a private setting for a group of opiate abusers is studied.
Methods: A total of 226 male opiate dependent clients (mean age 37.1 ±11 years) referring to a private treatment service in Tehran, entered the study. The majority of patients (72.6%, n=164) were opium abusers. The clients were initially stabilized on an equivalent dose of TO and in case of consent, their doses were tapered by 10% every 21 days. In addition to TO all individuals participated in self-help programs including peer counseling and recreational activities initiated by Congress 60, an NGO for opium abusers.
Results: After 12 months of follow up, 37 (16.4%) of cases had dropped off treatment and had relapsed to illicit drug use. Twenty-two (9.8%) had voluntarily tapered their TO and abstained from any licit or illicit opiate use, as confirmed through urine analysis. After a year, 167 clients (74%) continued to receive TO on a daily basis. No important side effect was met in the sample.
Conclusions: TO substitution seems a viable alternative to MMT and BMT in a selected group of individuals. In the Iranian classical medicine, substitution on opium and its gradual tapering has been endorsed for more than 4 centuries as a cure for opium addictions and public opinion strongly favors such an initiation. Currently many NGOs and public figures support such an approach and TO treatment might turn to an acceptable method for the large number of opiate abusers in Iran as well as users in neighboring countries especially Afghanistan who share common cultural beliefs and practices.
Financial Support: No financial support received.

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THE EFFECT OF THE LIFE ENHANCEMENT TREATMENT FOR SUBSTANCE USE (LETS ACT) ON COCAINE RELAPSE: RESULTS FROM A RANDOMIZED CONTROL TRIAL.

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Aims: Depression is a frequent comorbid condition among drug users, and previous work indicates that this comorbidity is significantly associated with increased rates of treatment dropout and substance use relapse. The Life Enhancement Treatment for Substance Use (LETS ACT) is a behavioral activation treatment for depressed substance users, and has demonstrated effectiveness in reducing depressive symptoms and rates of substance use treatment dropout. The current study expanded previous work by comparing LETS ACT to a control condition and examining the effects of treatment on substance use relapse.
Methods: 155 adults (*M* age = 41.6 years, 92.4% African American, 63.7% Male) with elevated depressive symptoms (Mean BDI Score = 13.1, SD = 6.0) were recruited from an urban inpatient substance abuse treatment center. Participants were randomized to receive LETS ACT or supportive counseling (SC), a nondirective time-matched control treatment. Substance use outcomes were measured via urinalysis at one month post-treatment. The retention rate for the 1-month follow-up assessment was 81.9% (n = 127).
Results: Demographics, drug use, and depressive symptoms were equivalent at baseline across treatment conditions. Intent-to-treat logistic regression analyses revealed that treatment condition significantly predicted cocaine use at the 1 month follow-up (*OR* = 4.45, *CI* = 1.0-9.7, $p < .05$); 19.2% of individuals in SC tested positive for cocaine use compared to 5.4% in LETS ACT.
Conclusions: Results indicate that LETS ACT is associated with significantly lower rates of cocaine relapse compared to a supportive control treatment condition. LETS ACT emerges as a feasible and straightforward intervention that can be disseminated to improve inpatient substance use treatment outcomes. Future directions, including potential mechanisms of change, will be discussed.
Financial Support: This work was supported by the National Institute for Drug Abuse (R01DA026424; PI: Daughters and F31DA026679; PI: Magidson).

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TIME-DEPENDENT IMPACT OF TRAUMATIC BRAIN INJURY ON THE BEHAVIORAL EFFECTS OF COCAINE.

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Aims: The aim of this experiment was to investigate the relationship between traumatic brain injury (TBI) and substance use disorder, which commonly co-occur. We hypothesized that the locomotor stimulatory effects of cocaine would increase after TBI.
Methods: Using moderate fluid-percussion injury, male Sprague-Dawley rats (N=12) received either TBI (n=6) or sham injury (n=6) under isoflurane anesthesia. On post-injury day 2 (PID2), rats were habituated to the activity monitors and the injection procedure. On PID3, rats (n=3/condition) were habituated for 30 min prior to injection of saline (1 ml/kg, ip) or cocaine (15 mg/kg, ip) and locomotor activity was monitored for 120 min. All rats were challenged with cocaine again and activity was monitored for 120 min on PIDs 13, 20 and 34. Stereotyped behavior was assessed 10-15 min post-injection via a modified Kilbey-Ellinwood rating scale. Data were analyzed by two-tailed Student's t- Test (α=0.05).
Results: On PID 3, cocaine induced significant hyperactivity vs. saline treatment in sham-injured rats ($P<0.05$). The response to cocaine was reduced after TBI, as there was no significant difference in hyperactivity in cocaine- vs. saline-treated TBI rats (P=0.32), and a trend toward reduced activity in cocaine-treated rats, TBI vs sham (P=0.07). On PID 13, in rats previously saline-treated, the mean activity in response to cocaine was lower in injured rats compared to uninjured rats, although not statistically significant. However, cocaine induced significant hyperactivity in injured rats on PID20 compared to PID13 ($P<0.05$) and showed a trend toward increased activity on PID32 compared to PID13 (P=0.07). In comparison, sham-injured rats showed no differences in their response to cocaine on PIDs 13, 20 and 34.
Conclusions: The locomotor stimulatory effects of cocaine are reduced when assessed early after TBI, but are enhanced at later time points after injury.
Financial Support: The Moody Center for Traumatic Brain & Spinal Cord Injury Research/Mission Connect and the UTMB Center for Addiction Research

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LONG-ACTING COCAINE ESTERASE (LACE): ASSESSING THE TREATMENT APPROACH.

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Aims: No medications have been approved for the treatment of cocaine dependence. The aim of this work was to determine the need for and commercial viability of a high turn-over cocaine esterase with high specificity and selectivity with activity for 2-4 weeks after subcutaneous injection for treatment of cocaine dependence.
Methods: The Technology Transfer Office, University of Michigan requested an independent assessment of the commercial viability of this treatment approach based in part on Collins GT et al., Neuropsychopharmacology. 2012 ;37:1092-103. Thirteen internationally recognized clinical, policy and research leaders in the addiction field participated in a structured phone interview. Six were former CPDD Awardees.
Results: Direct quotes - Need: "no benefit from medications; little benefit from outpatient treatment; some benefit from in-patient treatment ; but nothing works". LACE would be a "substantial advance" and "preferred treatment" if patients would take for at least 6 months. "It takes 2 years to get your life back"
Advantages: "solves the compliance problem" and "removes the reinforcing effects of cocaine" "so over time other interventions can work"
Target patients: "Any one who was motivated"; approvable indication and label "relapse prevention" .
Reimbursement: "would follow as it has for buprenorphine and naltrexone". "higher functioning professionals with a lot to lose would pay directly"; "Accountable/ Managed Care and HMOs ". "The Affordable Care Act will help"
Challenges: "patient acceptance"; "antibody formation"; "poly-drug use"; "injection volume"; "need physician involvement"; "few funding sources"; "regulatory requirements"; "cost of medication".
Market size: Probably $200-350M 3 years after approval and launch
Conclusions: LACE is potentially a superior treatment approach to cocaine dependence, commercially viable and addresses an unmet public health need. Substantial development challenges exist. Government support, an expedited efficacy development plan focused on safety combined with post-marketing studies might be considered.
Financial Support: Technology Transfer Office, University of Michigan.

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EATING HIGH FAT CHOW INCREASES SENSITIVITY OF FEMALE RATS TO INDIRECT-ACTING BUT NOT DIRECT-ACTING DOPAMINE RECEPTOR AGONISTS.

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Aims: Diet can impact sensitivity to drugs that act indirectly (i.e. cocaine) or directly (i.e. quinpirole) on dopamine receptors. Eating high fat chow increases sensitivity of female but not male rats to cocaine-induced locomotion and sensitization. Eating high fat chow increases sensitivity of male rats to quinpirole-induced yawning and results in insulin resistance; it is not known whether this diet has similar effects in females.
Methods: Female Sprague-Dawley rats had free or restricted access (i.e., body weight matched to standard chow fed controls) to high fat chow (34.3% fat) or free access to standard chow (5.7% fat).
Results: Quinpirole (0.0032-0.32 mg/kg) dose-dependently induced hypothermia and modest rates of yawning. Despite the development of insulin resistance within just 10 days of eating high fat chow, quinpirole dose-response curves for yawning and hypothermia were unchanged over 7 weeks of access to high fat chow (both groups) or standard chow. Rats eating high fat chow were more sensitive to cocaine-induced (1-17.8 mg/kg) locomotion; however, rats eating standard chow also became sensitive following repeated administration of cocaine.
Conclusions: That eating high fat chow increased sensitivity of female rats to indirect-acting, but not direct-acting dopamine receptor agonists suggests that eating high fat food might increase vulnerability to abuse drugs like cocaine, particularly among females.
Financial Support: CPF is supported by the NIDA Senior Scientist Award (K05 DA017918).

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DOES CRAVING PREDICT SUBSTANCE USE FOR DIFFERENT SUBSTANCE USE DISORDERS? AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY IN PATIENTS WITH ALCOHOL, TOBACCO, CANNABIS AND HEROIN DEPENDENCE.

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Aims: The objective of this study was to assess substance-dependent patients in their natural environment using Ecological Momentary Assessment (EMA) to examine the prospective association between craving and substance use.
Methods: A total of 132 participants beginning treatment for addiction were recruited from an outpatient treatment center and completed 2 weeks of computerized ambulatory monitoring of daily life experiences. The main substance of dependence was alcohol (n=39), opiates (n=32), tobacco (n=32), or cannabis (n=29). Patients were asked to describe in real-time their experience of craving and substance use. Data were analyzed using hierarchical linear models (HLM).
Results: Craving intensity was strongly predictive of use of the substance that initiated treatment, whether substance use was measured during the same assessment (γ = .429, p<10-4), or prospectively over the subsequent 3-hour period (γ = .137, p=0.002). When the prospective models were adjusted for initial substance use, craving remained a significant predictor of substance use over the subsequent 3-hour period (γ = .137, p=0.002). These effects were equivalent for men and women, and did not differ by type of substance use disorder. This association was no longer significant for substance use 6 hours later (γ = .035, p>0.05). Substance use was also examined as a predictor of later craving intensity, but the association was not significant when adjusting for initial craving levels.
Conclusions: This study highlights the central role of craving in determining substance use during quit attempts for a wide variety of substances (legal/illegal, stimulant/sedative).
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008, CNRS ATIP.

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CONTENT VALIDATION OF THE PRESCRIPTION OPIOID MISUSE, ABUSE, AND DIVERSION (MAD) INSTRUMENT IN THE CHRONIC PAIN PATIENT POPULATION.

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Aims: Despite the growing problem of prescription opioid misuse, abuse, and diversion (MAD) in society, the prevalence of MAD in the pain patient population is not clear. Since there are no instruments that measure MAD in this patient population, a novel, self-report MAD Instrument has been developed. This instrument assesses tampering methods, overconsumption, use by unintended routes of administration, and diversion. The instrument queries the motives behind these behaviors in order to classify them as either misuse or abuse. The MAD Instrument consists of several questions with multiple-choice options, and several questions where patients rate their concerns regarding prescription opioids on an 11-point (0 = not at all to 10 = extremely worried) numeric rating scale. This study assessed the content validity and patient interpretation of the MAD Instrument.
Methods: Patients with chronic pain, who were at low risk for prescription opioid abuse and were currently taking opioids for optimal analgesia (≥ 30 days) have undergone 2 rounds of 1:1 cognitive interviews (round 1, n=9; round 2, n=11). Participants also completed sociodemographic and Brief Pain Inventory questionnaires.
Results: Patient age ranged from 25 to 76 years, 60% were female, and 80% white. Overall, 17 (85%) patients reported feeling comfortable answering the questions honestly. Five (25%) patients stated concerns regarding confidentiality and legal consequences when completing the questionnaire via internet and 3 did not have internet access. Six (30%) did not understand the term "opioid"; the use of "strong pain medication" was clearer. Participants understood the meaning of each question and were not offended. Participants were able to answer questions with the given response options. For reasons of misuse/abuse, obtaining pain relief quicker or better were suggested as reasons to include.
Conclusions: Overall, the patients understood the MAD Instrument and could answer its questions.
Financial Support: This study was sponsored by Pfizer Inc.

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AGE TRENDS IN ABUSE CALLS TO POISON CENTERS INVOLVING PRESCRIPTION OPIOIDS.

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Aims: The purpose of this study was to examine correlates and differences in the peak age in years of intentional abuse calls to poison centers mentioning different classes of prescription opioids.
Methods: Data from the RADARS® System Poison Center program were used. Mentions of prescription opioid drug classes by intentional abuse cases from the 1st quarter of 2010 through the 2nd quarter of 2012 were summed by age between the ages of 11 years and 69 years. A linear regression model tested the association between the age with the greatest number of mentions (peak age) for each drug and the log of number of individuals filling a prescription for that drug. A negative binomial regression was used to fit a growth curve to each prescription opioid class to examine differences in age trends by drug.
Results: Findings suggest a statistically significant (R2 =0.56, p=0.032) inverse association between peak age of intentional abuse calls to poison centers and drug availability. Hydrocodone, oxycodone, and tramadol were the most available drugs and had peak abuse ages under 22. Methadone and hydromorphone were less available and had peak abuse ages over 23. Growth curve modeling yielded statistically significant differences in age trends of intentional abuse exposures by drug class. Differences in the total number of abuse exposure mentions between drugs were greatest prior to age 20.
Conclusions: Younger abusers who are more likely to be in the early stages of drug abuse are likely to abuse opioid medications that are readily available. Most intentional abuse calls involve cases under the age of 30 and primarily involve hydrocodone, oxycodone, and tramadol. After age 20, differences between drug classes are less pronounced.
Financial Support: The RADARS ® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscription from pharmaceutical manufacturers.

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THE EFFECTS OF THE INTERACTION BETWEEN BODY WEIGHT AND DEPRESSION ON ADOLESCENT AND EMERGING ADULT ALCOHOL USE.

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Aims: Researchers have suggested that obese individuals consume alcohol at a lower rate than that of the general population, and that alcohol dependence can be linked to depression. However, seemingly counter-intuitively, obesity has also been associated with depression. The present study aimed to address these findings by examining whether body weight and depression interact in such a way as to effect alcohol use in adolescents.
Methods: We used a two-way Analysis of Variance (ANOVA) to examine the data gathered from participants concerning their frequency of alcohol use, weight status (Healthy weight or Overweight / Obese) via their body mass index, and self-reported levels of depression. The study utilized a sample composed of adolescents and young adults (N = 43).
Results: Our results showed that the interaction between depression and body weight status had an effect on the rate of alcohol consumption in study participants [F (1, 42) = 4.837, p < .05]. Our results indicated that healthy weight individuals who scored low on depression were ranked high in alcohol consumption (M = 2.82), followed by overweight / obese individuals who scored high on depression (M = 2.33), then by healthy weight individuals who scored high on depression (M = 1.91). Overweight participants who scored low on depression also scored the lowest on rate of alcohol consumption (M = 1.67).
Conclusions: These findings indicate that body weight status and depression interact in such a way that they influence the rate of alcohol consumption in adolescents and emerging adults. One possible explanation is that non-depressed, healthy weight individuals may engage in higher levels of social drinking than do their overweight peers. However, if the healthy weight individual is depressed, they may forgo these social outings. Obese individuals, who presumably are more impulsive, may be more likely to use drinking as a coping mechanism for their depression than are their healthy weight peers.
Financial Support: The study was financially supported by Dr. Sherecce Fields' faculty start-up funds.

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COMPARING RESULTS FROM TWO SMOKING CESSATION TRIALS THAT USED PARTICIPATORY RESEARCH METHODS.

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Aims: Smoking cessation programs in low-income populations have relatively lower recruitment, retention, and success rates. A barrier to improvement is the minimal involvement of community stakeholders in the design, implementation, and evaluation of the services. We compare outcomes from two interventions of a Community-Based Participatory Research initiative.
Methods: Two studies using randomized assignment to usual or enhanced care have been implemented (Phases 1 and 2). The treatment effects were evaluated through self-reported smoking abstinence verified by expired-air carbon monoxide (CO). In Phase 1, the interventions were delivered by trained staff of a Community-Based Primary Healthcare Center. In the Phase 2, the programs were implemented at community settings and through Peer Motivators. A total of 543 participants have been recruited (41% women; 62% African Americans, 29% Whites; 66% were 40 years or older, 50% did not have a job).
Results: Results of "Phase I" showed improvement compared to baseline measurements and to the experience prior to the partnership by the Clinic. In total, nearly 400 individuals participated in the program with an almost 9% rate of smoking cessation (8.9% and 8.6%, for the "standard care" and "enhanced group intervention" groups, respectively). Only 14% of the participants attended between 6 to 12 sessions but they had much higher quit rates (27%) compared to those who attended fewer than 6 sessions (6%, p<0.001). In contrast, preliminary data indicate higher retention in Phase 2 (between 50 to 75 percent) and higher cessation rates (between 30-50 percent).
Conclusions: Community engagement in the design, implementation and evaluation of a smoking cessation program involving Community Peer Motivators can be successful among low income populations.
Financial Support: Supported by grant 5 R24 MD002803 from the National Center of Minority Health and Health Disparities

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ANTI-METHAMPHETAMINE VACCINE ATTENUATES BRAIN LEVELS AND LOCOMOTOR ACTIVITY OF METHAMPHETAMINE IN MICE.

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Aims: A vaccine is being developed as a treatment for methamphetamine (MA) dependence. The immunogenicity of the conjugate vaccine (Tetanus toxoid- succinylmethamphetamine, TT-S-MA) was evaluated, in the presence and absence of adjuvants (E6020 or E6020 plus alum), to determine if this vaccine would generate MA antibodies, reduce the MA levels in brain, and alter MA-induced behavior.
Methods: Mice were vaccinated at 0, 3 and 18 weeks using 0, 10, 30 or 100 μg conjugate vaccine adsorbed to E6020 adjuvant (a synthetic monophospholipid), or E6020 plus aluminum. Antibody responses were measured at bi-weekly intervals by ELISA. At 7 and 13-wks, locomotor activity was assessed in 90-min sessions after MA administration at dose 0.5 or 4 mg/kg, respectively. The effect of TT-S-MA on the pharmacokinetics of MA (4 mg/kg) was determined by measuring the MA levels in brain and blood using gas chromatography/mass spectrometry.
Results: Serum antibody was detected at 2-wk, reached peak levels by 4 wks, and remained at moderate to high levels until 18-wk, and peaked again at 22-wks after the second boost. Non-vaccinated mice showed MA dose-dependent activity effects with hypolocomotion at the 0.5 mg/kg dose and elevated activity levels at the 4 mg/kg dose. Both dose effects were reduced in TT-S-MA groups, particularly in mice that received 10ug vaccine with E6020 plus aluminum. In addition, immunized mice displayed 40% lower levels of methamphetamine in the brain and a 43% increase in the relative blood levels following MA injection. This indicates that the MA was being retained in the blood rather than entering the brain or other organs.
Conclusions: We have shown that TT-S-MA can produce sufficient antibody levels to reduce brain levels of MA and to attenuate the locomotor activity of MA in mice.
Financial Support: DP1DA033502.

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EFFECTS OF LIPOPOLYSACCHARIDES ON DOPAMINE-RELATED BEHAVIOR OF METHAMPHETAMINE.

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Aims: Methamphetamine (METH) is one of the most addictive psychostimulants that dramatically changes the central nerves system functions. Various studies have reported to support substantial roles of mesolimbic dopaminergic pathway, which projects from the ventral tegmental area to the nucleus accumbens, in the rewarding effects of psychostimulants. It has been demonstrated that changes of immune functions can affect an establishment of reinforcing/rewarding effects of abused drugs. Particularly, we previously demonstrated that lipopolysaccharide (LPS), which activates the immune function, can abolish the establishment of rewarding effects of cocaine, however, the role of immune functions in the establishment of rewarding effects induced by abused drugs has not been fully elucidated yet. Therefore, the present study was designed to investigate the effects of activation of immune functions in the establishment of rewarding effects of methamphetmaine.
Methods: METH (1 mg/kg, s.c.)-induced rewarding effects in mice were measured by conditioned place preference paradigm. The locomotor activity of mice was measured by an ambulometer. Total activity counts were automatically recorded for 3 hr after the injection of METH (1 mg/kg, s.c.).
Results: Consistent with the previous results, METH (1 mg/kg, s.c.) produced the robust rewarding effects in mice as measured by conditioned place preference paradigm, whereas these effects induced by methamphetmaine were significantly suppressed by LPS (1 mg/kg, i.p.). Moreover, LPS inhibited the METH-induced hyperlocomotion. In these conditions, LPS could activate the microglia in the nucleus accumbens (NAc), and increase in the IL-1β, IL-6 and TNF-α mRNA levels, whereas METH did not produce any change for the activation of microglia or these mRNA. Furthermore, up-regulation of phospholyrated-CREB by methamphetmaine was inhibited by LPS.
Conclusions: These results suggest that activation of immune system induced by LPS is involved in the suppression for dopamine-related behaviour induced by METH.
Financial Support: Tsutomu Suzuki

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DIFFERENCES IN EARLY SUBSTANCE USE AND RISK FACTORS BY ASIAN-AMERICAN PACIFIC ISLANDER (AAPI) SUBGROUPS.

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Aims: Epidemiological studies of adolescent substance use frequently group AAPIs together which neglects the heterogeneity in risk by subgroups. This study examines differences in lifetime substance use, initiation of substance use over a three year period, and risk factors for alcohol, cigarette, and marijuana use among seven subgroups of AAPI adolescents. It represents the first longitudinal study of an adolescent population with the most subgroups of AAPIs and the youngest sample studied to date.
Methods: Sixth and seventh grade AAPI adolescents (n=901) in Southern California were surveyed over five waves through 8th and 9th grades. Using ANOVA and chi square tests, we examined subgroup differences in (1) lifetime alcohol, cigarette, and marijuana use, (2) initiation of each substance over three years, and (3) baseline individual (positive and negative beliefs about substances, resistance self-efficacy, intentions to use), family (closest adult and older sibling substance use), and school factors (perceived peer use).
Results: Although there was great heterogeneity in lifetime substance use and initiation rates, subgroup differences were not statistically significant (p>0.20). Negative beliefs about cigarettes (p=0.003) and marijuana (p= 0.018) differed by subgroup such that Chinese adolescents had the highest negative beliefs; Japanese and Vietnamese adolescents had the lowest negative beliefs about cigarettes and marijuana, respectively. Vietnamese adolescents reported the highest levels of perceived peer cigarette use and Koreans reported the lowest (p=0.003). Japanese and Vietnamese adolescents reported the highest frequency of alcohol (p=0.001) and cigarette use (p=0.004) by their closest adult, respectively.
Conclusions: Significant subgroup differences existed for negative beliefs about use, perceived peer use, and close adult use. Although no differences in substance use or initiation rates were observed, these findings are an important first step in understanding heterogeneity in AAPI adolescents' risk for substance use and initiation.
Financial Support: Supported by NIAAA R01AA016577 (D'Amico)

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PATTERNS AND SETTINGS OF 3, 4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA) USE AT DANCE PARTIES IN JAPAN.

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Aims: To examine the patterns of use of MDMA at dance parties in Japan and the various settings where it is used.
Methods: An anonymous self-administered questionnaire survey was conducted using laptop computers at 4 dance parties at 2 different clubs in Tokyo, Japan. The questionnaires were completed by 237 partygoers. Twenty-nine participants who reported that they had already answered the survey were excluded from the dataset. Data from the remaining 208 (39.9% women; 42.8% aged 25–29 years) participants were analyze.
Results: A total of 9.1% of participants reported MDMA use. The drug-use patterns that were reported among participants included "use in out-of-rave settings" (19.2%),"use before parties" (16.8%) and "use at parties" (13.9%). "MDMA users" were significantly more likely than "cannabis users" (non-MDMA users who had used cannabis) to use drugs before the parties began (p = 0.001). Among participants who used drugs at parties, MDMA users were significantly more likely than cannabis users to use drugs on the dance floors (p = 0.002) and in the lounges (p = 0.005) of clubs. However, no statistically significant difference was found between MDMA and cannabis users regarding drug use in bathrooms and VIP rooms.
Conclusions: Our results suggest that MDMA users are likely to use drugs before entering parties in order to keep their drug use secret, as the identities and personal belongings of visitors are often checked at clubs in Japan. However, once drugs are brought into parties, MDMA users are likely to use them on dance floors and in lounges. Cannabis needs to be lit and produces smoke, while MDMA is typically contained in a colorful tablet that is taken orally. Therefore, MDMA users may prefer to use the drug in public spaces at parties, such as dance floors and lounges.
Financial Support: This work 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.

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CHILDHOOD PHYSICAL ABUSE, SENSITIVE PERIODS, AND PROBLEMATIC ALCOHOL USE IN YOUNG ADULTHOOD.

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Aims: Childhood physical abuse (CPA) has been linked to problematic alcohol use in young adulthood, but there is a paucity of empirically-based knowledge on how timing of the insult influences different drinking behaviors in young adulthood. We examine the utility of two different characterizations of CPA timing to predict later drinking behaviors. We hypothesize that the drinking-related sequelae of CPA would depend, at least in part, on the timing of the physical abuse.
Methods: Using a community sample of young individuals (N=297; mean age: 21.9; female 60%), we performed latent class analyses (LCA) to identify homogenous groups of young people with similar patterns of CPA timing. Timing of CPA was also characterized in terms of developmental periods (i.e., infancy/preschool, middle childhood, adolescence). Multiple linear and logistic regression models were used in an effort to examine the associations between CPA timing and four types of drinking behaviors including drinking frequency, binge drinking, alcohol-related problems, and alcohol use disorder (AUD).
Results: LCA identified three heterogeneous classes of young people distinguished by quantitative differences in CPA timing (i.e., no CPA, post-pubertal CPA, chronic CPA). Chronic CPA was associated with all drinking behaviors ($\beta = 0.45 – 0.88$) with the exception of AUD, whereas post-pubertal CPA was associated with drinking frequency ($\beta = .41$) and binge drinking (odds ratio = 2.74). Our analyses also revealed that physical abuse that has occurred in adolescence predicted drinking frequency ($\beta = .52$) and alcohol use problems ($\beta = .58$).
Conclusions: The present study suggests that timing of CPA may play a significant role in linking CPA to problematic alcohol use in young adulthood. The results of this research suggest that adolescent physical abuse and chronic CPA are particularly related to drinking behaviors in young adulthood.
Financial Support: This research was supported by NIDA DA030884 and the ABMRF/The Foundation for Alcohol Research.

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DIFFERENTIAL ALTERATION IN α3-CONTAINING GABA A RECEPTORS AFTER LONG-TERM COCAINE SELF-ADMINISTRATION IN RHESUS MONKEYS.

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Aims: We have shown previously that rhesus monkeys self-administering cocaine show alterations in both α1 and α2 subunit-containing GABAA receptors in reward related nuclei. In addition to α1 and α2-containing GABAA receptors, α3-containing GABAA receptors have been implicated in reward processes. The aim of the present study is to examine α3 subunits of the GABAA receptor (α3GABAA receptor), using immunohistochemistry (IHC), in reward-related nuclei (nucleus accumbens, NAc; ventral tegmental area, VTA; anterior cingulate cortex, ACC; caudate, Cd; and putamen, Put) after long-term cocaine self-administration.
Methods: Ten male rhesus monkeys either self-administered cocaine intravenously (1-hr/day, 0.03 mg/kg/injection of cocaine) or received passive infusions of saline yoked to the cocaine injections (yoked control) for ~100 days (Mean: 109 +/- 11 days). Twenty-four hours after the last session, animals were sacrificed and their brains removed. The tissues were cryosectioned and IHC was conducted using a commercially available antibody to the α3 subunit. Staining intensity was measured in regions of interest (ROIs) using ImageJ software
Results: We found significantly higher immunoreactivity for α3 subunits within the NAc in cocaine-exposed monkeys compared to yoked controls, whereas no corresponding effects were found in the ACC and VTA. Within the Cd, we found significantly lower staining for α3 subunit immunoreactivity in cocaine-exposed animals. In contrast, within the Put, we found significantly higher levels of immunoreactivity in cocaine-exposed monkeys in comparison to controls.
Conclusions: Our results suggest long-term exposure to cocaine can differentially alter α3 subunit immunoreactivity within the NAc, Cd, and Put. These changes may reflect compensatory mechanisms resulting from chronic cocaine-induced over-activation of DA neurons. The α3GABAA receptor subtype may provide a potential target for pharmacotherapy development to treat cocaine addiction.
Financial Support: DA011792, DA033795, AG035361, OD011103

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FAAH GENOTYPE AND MJ USE PREDICT EXECUTIVE FUNCTIONING IN ADOLESCENTS AND EMERGING ADULTS.

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Aims: Marijuana (MJ) use continues to increase (Johnston et al., 2012) and has been associated with impairments in complex attention and executive function in youth (Lisdahl et al., 2012). The gene coding for Fatty Acid Amide Hydrolase has been linked with endogenous cannabinoid (CB) signaling (FAAH; Glaser et al., 2003). Here, we examine whether FAAH genotype interacts with MJ use to predict executive function (EF) in youth.
Methods: Data were collected from (ages 18-25) 39 MJ users and 44 controls. Of those, 28 were FAAH A carriers and 55 were homozygous (C/C) carriers. Exclusion criteria included co-morbid psychiatric and neurologic disorders; excessive other drug use. Subjective data of EF was measured by the Frontal Systems Behavior Scales (FrSBE; Grace & Mallory, 2001). The Ruff 2 & 7, PASAT and Wisconsin Card Sorting Task (WCST) measured EF and complex attention. Multiple regressions were used to predict EF indices from past year MJ, FAAH status, and MJ*FAAH interactions controlling for demographic variables and comorbid drug use.
Results: After controlling for potential confounds, MJ use significantly predicted greater Executive Dysfunction (beta=.30, p=.02) and marginally greater Disinhibition (beta=.21, p=.10). Significant interactions between MJ*FAAH were seen in predicting Executive Dysfunction (beta=.21, p=.05), Disinhibition (beta=.41, p<.001), and Apathy (beta=.29, p=.009) scores; marginal interactions were seen with complex attention (Ruff 2&7: beta=.17, p=.10; PASAT: beta=.18, p=.06). FAAH A carriers had marginally higher Apathy (beta=.19, p=.09) and complex attention (beta=.17, p=.11) scores.
Conclusions: We found divergent genetic prediction of executive functioning in a sample of adolescent MJ users. Despite lower drug use, carriers of FAAH A reported greater EF symptoms; insight into cognitive problems observed with FAAH A allele carriers may actually be protective. Consistent with Haughey et al (2008), carriers of FAAH 385C demonstrated lowered complex attention. Additional interpretations and implications will be discussed.
Financial Support: 1 R01 DA030354-01; PI: Lisdahl.
1R03 DA027457-01; PI: Lisdahl

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ASSOCIATION BETWEEN α-1 ADRENERGIC RECEPTOR (ADRA1A) GENOTYPE AND SUBJECTIVE COCAINE EFFECT IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: We examined whether a functional variant of the ADRA1A gene enhances the subjective effects of cocaine in a group of cocaine dependent individuals.
Methods: This study is a within-subject, double blind, placebo-controlled inpatient human laboratory evaluation of 46 non-treatment seeking cocaine dependent (DSM-IV) subjects, aged 18yr to 55yr. Participants received both placebo (saline, IV) and cocaine (40mg, IV), and subjective responses were assessed 15 minutes prior to receiving cocaine and at 5-minute intervals for 20 minutes following cocaine administration. We then genotyped the rs1048101 ADRA1A variant and evaluated whether the Cys to Arg substitution at codon 347 in exon 2 (Cys347Arg) was associated with the subject's rating of cocaine effect.
Results: Nineteen (41%) subjects were found to have the major allele CC genotype, and 27 (59%) carried at least one T allele of rs1048101 (TT or TC genotype). Significant between group differences in subjective effects were observed for "Cocaine Desire" ($p < 0.05$) and for "Cocaine Liking" ($p < 0.05$), with those in the CC genotype reporting higher ratings of drug desire and drug liking. In addition, although there was no statistically significant difference between groups in regards to baseline depression score, the CC group also reported higher depression scores after receiving cocaine infusion ($p = 0.03$).
Conclusions: The CC genotype of ADRA1 was found to be associated with elevated ratings of cocaine desire and liking. This study indicates that ADRA1A genotype could be used to identify a subset of individuals for whom cocaine may be more rewarding.
Financial Support: Funding for this study was provided by NIDA Grant 5 P50 DA018197-07 (TRK).

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HIV RISK BEHAVIORS AMONG RETURNEE MALE MIGRANT WORKERS IN NEPAL.

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Aims: Background: Seasonal migration of Nepali male workers to India is common in Nepal. Unsafe sexual activities and drug use behaviors of these migrants in India and after returning to Nepal, has led to a high HIV prevalence among this subgroup. This study was designed to explore consequential risk behaviors that contribute to migrant workers' vulnerability to HIV infection and transmission.
Methods: Methods: We performed a systematic review of literature focused on "HIV risk behaviors of male labor migrants". Records were collected from electronic databases, web-based searches, and national and international reports.
Results: Results: HIV prevalence in Nepal, though it decreased from 8.5% in 2002 to 1.1% in 2008, is still very high among male migrant labor workers and rates are rapidly trending higher in association with increased high-risk behaviors in this group. A startling 41% of all HIV infections in Nepal are among male migrant workers. This review found that migrant workers commonly exhibit HIV risk behaviors such as having multiple sex partners, inconsistent condom use, unsafe drug use, and alcohol use disorders. Furthermore, we found that they have substantial deficits in knowledge of HIV/STIs, and safe sex and safe drug use skills.
Conclusions: Conclusions: Our findings suggest that migrant labor workers are at extraordinary risk for acquiring and transmitting HIV infection because of higher prevalence of HIV risk sexual and drug use behaviors. This review suggests the need for a comprehensive HIV program addressing safe sex and drug use habits directed toward migrants labor workers in order to reduce the risk of spreading HIV.
Financial Support: Funding Source: University of Connecticut, College of Liberal Art and Sciences (Christine N. Witzel Award)

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ATTENUATION OF DEPRESSIVE SYMPTOMS ASSOCIATED WITH MTHFR DURING A COCAINE VACCINE TRIAL.

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Aims: This study assessed whether a cocaine vaccine that reduced cocaine use interacted with a genetic variant of the methylenetetrahydrofolate reductase (MTHFR) gene to reduce depression levels in cocaine and opiate dependent patients.
Methods: This 14-week randomized clinical trial assessed depression scores using a modified version of the Center for Epidemiological Studies Depression scale (CES-D) and cocaine positive urine percentages in 64 cocaine and opioid co-dependent subjects on methadone. We genotyped the rs1801133 MTHFR variant and evaluated whether the C to T mutation at the C677T polymorphic site was associated with the subject's depression and cocaine use.
Results: Depression scores for the TT genotype patients were elevated at 2.7 during the 4-week baseline and decreased to 0.4 for the TT vaccinated group, while depression scores remained elevated for the TT placebo group. The CC and CT genotypes group were 0.8 for the vaccine and 1.4 for the placebo group at baseline, and remained low throughout the study. Cocaine positive urines decreased from 81% to 45% for the TT vaccine group and remained near baseline levels of 60% for the TT placebo group. The change in CES-D scores was positively correlated with the change in cocaine-free urines for the TT patients ($r = 27.1$), and co-varying for the change in cocaine-free urines eliminated the association of increased depression symptoms with vaccine treatment and the MTHFR polymorphism.
Conclusions: The TT genotype of MTHFR was found to be associated with elevated depressive symptoms, and these symptoms dropped with a reduction in cocaine use suggesting that elevated homocysteine levels from cocaine use with the TT variant may produce depressive symptoms that resolve with reduced cocaine use.
Financial Support: Supported by: NIH/NIDA r0115477 (TK), for DN through MD Anderson's Cancer Center Support Grant DA026120 NIH/NIDA DA026120, the Veterans Health Administration, and the Toomim Family Fund.

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FINANCIAL INCENTIVES FOR SMOKING ABSTINENCE IN PATIENTS DIAGNOSED WITH PULMONARY DISEASE.

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Aims: Chronic obstructive pulmonary disease (COPD) is a serious respiratory illness predominantly caused by cigarette smoking. While smoking cessation is identified as the single most effective intervention to slow the rate of disease progression and reduce COPD-related mortality, abstinence rates following smoking cessation among COPD patients are notoriously poor. We have an ongoing pilot study investigating the initial efficacy of an intensive, incentive-based intervention for promoting smoking abstinence in patients with COPD.
Methods: Participants must report smoking >10 cigs/day, have a clinical diagnosis of COPD and have chronic airflow obstruction (post-bronchodilator FEV1/FVC<70%). Participants attend the clinic daily for 14 days and provide breath CO and urinary cotinine samples at each visit for monitoring of smoking status. Thus far, seven participants (54 yrs old, 29% male, 15 cigs/day, 53% FEV1/FVC) have been randomized to one of two experimental groups: Contingent participants (n=4) earn voucher-based incentives ($362.50 max) contingent upon biochemically-verified smoking abstinence and Noncontingent participants (n=3) receive vouchers independent of smoking status.
Results: While abstinence is generally high for both groups, preliminary analyses show a trend toward greater biochemically-verified smoking abstinence among Contingent vs. Noncontingent participants (68% vs. 50% negative samples, respectively; p=.11). By June 2013 we will have full data from the completed pilot study (n=20), including primary outcomes of biochemically-verified smoking abstinence as well as measures of nicotine withdrawal, craving and pulmonary functioning.
Conclusions: Overall, this pilot study is positioned to provide the first demonstration that smokers diagnosed with COPD can successfully quit smoking and inform efforts to develop an effective, longer-term smoking cessation intervention for this challenging and costly population of smokers.
Financial Support: Supported in part by T32 DA007242.

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DESOMORPHINE (CROCODILE) INJECTION AMONG IN-TREATMENT DRUG USERS IN TBILISI, GEORGIA.

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Aims: Aims: Since 2010 use of the opiate Dezomorphine ("crocodile") has increased dramatically in Georgia and neighboring countries. Crocodile is made in home-based laboratories, relatively new on the drug scene, and the risks associated with its use have not been studied. Here we present data on the prevalence and patterns of Crocodile use among a recent cohort of patients admitted for drug treatment in the Uranti clinic in Tbilisi, Republic of Georgia.
Methods: Methods: Secondary analysis of medical records and interviews with patients.
Results: Results: During the period (2011-2012), 220 patients (average age 32) were admitted to Uranti and among them, 80% (n=160) reported using crocodile for an average period of 7 months. Crocodile was described as a highly toxic drug prepared from different ingredients including codeine, iodine, gasoline and phosphorus and that causes severe damage to soft tissues and neurological complications when injected. Patients described its effects as short lasting resulting in multiple injections that averaged 3/day (range, 1-10). Group use of crocodile and sharing injection paraphernalia was reportedly widespread, as was combining crocodile with other drugs including methamphetamines (35%), and benzodiazepines and barbiturates (56%). During the study period one case of a crocodile related death caused by pulmonary embolism was recorded as were 3 cases of HIV (1.3%); 85% of patients tested HCV positive on admission to treatment.
Conclusions: Conclusions: Crocodile injection and sharing of injection equipment associated with its use is becoming widespread and has significant health risks. Further research is needed to better understand the risks and consequences of crocodile injection and develop effective interventions.
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EARLY ONSET CANNABIS USE AND YOUNG ADULT OUTCOMES: AN INTEGRATIVE DATA ANALYSIS OF THREE AUSTRALASIAN COHORTS.

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Aims: Investigation of the extent to which heavy early onset cannabis use is associated with later adverse outcomes is limited by sample size in existing cohort studies. Integrative data analyses may overcome this limitation. The study aimed to obtain more robust estimates of the effect of heavy adolescent cannabis use on particular life-course outcomes by age 25 years by developing integrative analyses across three large and long-running Australasian cohort studies (Australian Temperament Project, n=2443; Christchurch Health and Development Study, n=1265; Victorian Adolescent Health Cohort Study, n=2032).
Methods: A consistent metric for the measures of interest was identified across studies. Regression analyses were applied to integrated data to obtain pooled effect sizes adjusted for study effects and potential confounding factors.
Results: Results (OR, 95%CI) provide more robust estimates of the association between daily adolescent cannabis use and young adult outcomes including reduced educational attainment (0.3, 0.2-0.4) and increased depression (1.6, 1.1-2.4), self harm (3.8, 2.0-7.4), welfare dependence (1.7, 1.1-2.9), other illicit drug use (10.9, 7.7-15.6) and cannabis dependence (57.4, 37.7-87.6).
Conclusions: Results represent a significant advance over standard practice in meta-analysis by integrating data at the individual level. Findings demonstrate that the effects of daily adolescent cannabis use are pervasive across a number of domains.
Financial Support: The study was supported by an Australian Government National Health and Medical Research Council Project Grant.

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ALCOHOL USE AND RELATED PROBLEMS IN THE SãO PAULO MEGACITY MENTAL HEALTH SURVEY, BRAZIL: INFLUENCES OF NEIGHBORHOOD SOCIAL DEPRIVATION AND INDIVIDUAL SOCIOECONOMIC STATUS.

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Aims: To evaluate the influences of neighborhood social deprivation level (NSD) and individual socioeconomic status (SES) on alcohol use in a Brazilian population.
Methods: A probabilistic, multi-stage clustered sample of adult household residents in the São Paulo Metropolitan Area was analyzed (n=5,037). Past year alcohol use, regular use, heavy episodic drinking (HED, 4-5 drinks in one occasion), DSM-IV abuse and dependence were assessed with the CIDI for WMHS.
Results: Overall 12-month prevalences were 46% for alcohol use, 32.7% for regular use, 9.4% for HED, 2.7% for abuse, and 1.4% for dependence. For both genders, higher income levels were associated with increased odds for alcohol use and regular use. Among men, these odds were also increased for those unemployed or working/student when compared to retired/homemaker. Age between 18-54 years old, no/low NSD and being previously married were positive correlates of use and regular use among women. HED was associated with 18-54 years of age for both genders. High income and medium-low/medium NSD were positively associated with HED only among men, while being previously married was a significant correlate observed only for women. Alcohol dependence was more common among unemployed men and those living in medium-low/medium NSD when respectively compared with retired men and those living in no/low NSD. Unemployed women were at elevated risk for alcohol abuse.
Conclusions: Our results highlight that both NSD and individual SES may differentially influence men and women's alcohol use and problems. Further research should explore the causal mechanisms associated with alcohol use among women with no/low NSD and high income in developing countries as Brazil, while prevention policies should target HED pattern at younger ages as well as alcohol related problems among the unemployed, independently of gender.
Financial Support: State of São Paulo Research Foundation (FAPESP 03/00204-3). Center for Information on Health and Alcohol (CISA).

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THE IMPACT OF SUBSTANCE USE AND GENDER ON CONDOM USE SELF-EFFICACY IN A RURAL TREATMENT-SEEKING SAMPLE.

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Aims: The Condom Use Self-Efficacy Scale (CUSES) has been used with diverse populations as part of HIV prevention efforts. Previous research examining the relationship between substance use and condom use has been mixed. The present study investigated gender differences on the CUSES and whether substance use was associated with the CUSES at baseline.
Methods: Participants included 76 Native Americans seeking substance abuse treatment on a rural reservation. Participants completed the CUSES and the Addiction Severity Index (ASI; McLellan et al., 1992), as part of a randomized controlled trial of adapted motivational interviewing and community reinforcement approach. A scoring method for the CUSES (Barkley & Burns, 2000) was used and produced three scales: Appropriation, STD's, and Partners Reaction.
Results: Male and female Native American participants differed on two of the condom use self-efficacy scales. Specifically, males reported significantly higher confidence to purchase, carry, and use a condom (Appropriation) relative to female participants ($F(1, 74) = 5.40$, $p < .02$), but females reported significantly less discomfort about a partner's reaction to the use of condoms relative to males ($F(1,74) = 4.11$, $p < .05$). Frequency of cannabis use (past 30 days) was unrelated to any of the CUSES subscales while frequency of binge drinking days (past 30 days) was significantly and negatively related to less discomfort ($r = -.23$, $p < .05$). No gender by substance use interaction on CUSES subscale scores was observed.
Conclusions: Future intervention targets to increase women's condom use self-efficacy and decrease men's concern about partner reactions may be useful. Future investigation of the relationship between actual condom use skills and confidence levels as related to substance use may aid efforts to prevent STDs.
Financial Support: Supported by NIDA R01-021672

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LONGITUDINAL OUTCOMES OF MDMA (ECSTASY)-EXPOSED INFANTS IN THE UNITED KINGDOM.

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Aims: The present study assessed longitudinal outcomes in mental and motor development through 2 years in infants whose mothers used MDMA (Ecstasy) during pregnancy.
Methods: Pregnant women in the United Kingdom (28 MDMA uses; 68 non-MDMA users) were interviewed about recreational drug use and their infants followed from birth to 4, 12, 18, and 24 months of age. Assessments included the Bayley Mental and Motor Scales of Development (MDI, PDI) and mothers completed the HOME, the Brief Symptom Inventory (BSI) and the Drug Abuse Screening Test (DAST). Women were polydrug users, of middle socioeconomic status, average IQ, and in stable relationships. All but one MDMA user discontinued use after the first trimester and users were divided into heavier and lighter groups based on a median split. Infant birth parameters were not different except more MDMA infants were male. Effects of MDMA outcomes over time were assessed through a mixed model analysis, controlling for covariates of other drug use, HOME environment, and gender.
Results: There was a significant main effect of first trimester MDMA exposure on motor outcomes from 4 months to 2 years, ($F = 11.3$, $p < .002$) with more heavily MDMA-exposed children showing delays compared to lighter-exposed and non-exposed children (PDI = 90.8 (SE = 3.76) for MDMA vs.98.7 (SE = 1.39) for lighter and non-exposed at 2 years). Mental outcomes were not affected.
Conclusions: Prenatal MDMA exposure predicts poorer motor outcomes from 4 months to 2 years of age. Given the widespread recreational use of MDMA (Ecstasy), pregnant women should be cautioned about possible developmental effects in offspring.
Financial Support: Supported by grant DA14910-05 NIH – National Institute on Drug Abuse

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HUMANIZED MOUSE MODELS TO STUDY EFFECTS OF ANTI-COCAINE VACCINE.

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Aims: Initial vaccine formulation testing cannot be done in humans, and yet response characteristics in humans are often different than in lab animals. Therefore, human hematopoietic stem cells were transplanted into immunodeficient NOD–Rag1null IL2rγnull mice (Humanized-mice, Hu-mice). Hu-mice were vaccinated with conjugate vaccine against cocaine (tetanus toxiod-succinylnorcocaine; TT-SNC + Alhydrogel adjuvant) and were supplemented with plasmids expressing cytokines. The human specific cocaine antibody and locomotor responses to cocaine challenge were assessed at various time points.
Methods: Hu-mice were immunized with TT-SNC and received a booster dose 3 weeks later. Plasmids expressing GMCSF, IL-4 or IL-12 were delivered by a Genegun alone or in various combinations. Serum was assessed for human-specific anti-cocaine antibodies by ELISA. At 7 weeks, locomotor activity after cocaine challenge (15 mg/kg) was assessed.
Results: Anti-cocaine specific antibodies were detectable in the serum samples as early as 4 weeks, with a peak response at 6 weeks. In most cases, addition of cytokine expressing plasmids significantly increased antibody level over the group of mice immunized with TT-SNC alone that produced 848 µg anti-cocaine IgG/ml of serum (=1x). Maximum antibody was observed in the presence of GMCSF expressing plasmid (2.16x) followed by GMCSF + IL-4 combination (2.15x). The lowest antibody was produced in the presence of IL-4 + IL-12 and GMCSF (1.12x) followed by IL-12 (1.35x). There was a marked effect on the locomotor response in immunized mice, with substantial inhibition in the TT-SNC vaccinated mice and complete blockade of the response in the GM-CSF supplemented vaccinated mice.
Conclusions: Cocaine conjugate vaccine generated significantly high amount of human anti-cocaine IgG antibodies in this Hu-mice model, which was further increased in the presence of plasmids encoding various cytokines. Hu-mice showing maximum antibody level effectively blocked cocaine-induced locomotor responses.
Financial Support: DA023898, DA023898, DA030338, DP1DA033502.

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A LONGITUDINAL STUDY OF MARIJUANA USE MOTIVES ACROSS EMERGING ADULTHOOD.

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Aims: We examined the reciprocal influence of marijuana use motives (MJM) and marijuana use status across emerging adulthood. Endorsement of enhancement and social motives is higher among marijuana users than their nonusing peers and has been shown to relate to increased use among young adults cross-sectionally (Zvolensky et al., 2007). We anticipated that endorsement of MJM at one point in time would prospectively predict marijuana use status (nonuser/user) at a later point in time, above and beyond their current use status.
Methods: Using data from the Rutgers Health and Human Development Project (N=419), use status and MJM were assessed at ages 18, 21, and 28 years. MJM were categorized as positive reinforcement (social/enhancement; SE), negative reinforcement (coping/conformity; CC), or Expansion (EXP) categories. A path analytic model tested longitudinal relations between use status and MJM across time.
Results: The derived scales generally demonstrated a high level of reliability. As expected, MJM were positively associated with each other at each time point (rs = .14 to .85, ps = < .001). Concurrently, all motive categories were related to use status at age 18 (rs = .23 to .49, ps = < .0001) and age 21 (rs = .24 to .41 ps = < .0001). However, only SE motives were associated cross-sectionally with use status at age 28 (b = .14, p = .004). 22% of the variance in use status at age 21 was predicted by greater endorsement of SE motives at age 18, b = .28, p <.0001, and past use status (age 18), b = .32, p <.0001. By age 28, 33.7% of the variance in use status was accounted for by the longitudinal model; however, MJM were not significant predictors of use status at this time point.
Conclusions: We replicated previous research demonstrating that endorsement of MJM correlates with current use status and suggests that positive reinforcement motives for marijuana can predict future use of marijuana for emerging adults above and beyond previous use status
Financial Support: DA/AA 03395 to Pandina, Labouvie, & White; R01 AA 019511 to Mun & White

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GENDER DIFFERENCES IN SEXUAL ABUSE HISTORY AND HIV PREVENTION OUTCOMES AMONG TREATMENT-SEEKING SUBSTANCE ABUSERS.

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Aims: Many substance abusers engage in sexual risk behaviors associated with HIV infection. Sexual abuse is a strong predictor of HIV risk, and individuals with sexual abuse histories may benefit less from HIV prevention interventions. This study examined the impact of sexual abuse and gender on sexual risk behavior among treatment-seeking substance abusers.
Methods: Participants were enrolled in one of two gender-specific HIV prevention trials conducted by the NIDA Clinical Trials Network. Eligibility criteria were ≥18 years old, unprotected intercourse in the past 6 months, and current substance abuse treatment. Participants were randomized to a 5-session skills-building group treatment or a 1-session HIV information group. They reported past 3 month sexual behavior at baseline and at 3- and 6-month follow-ups.
Results: The sample included 378 women and 436 men. Women were more likely to report sexual abuse (59% vs. 19%, p<.001). At baseline, sexual abuse was associated with multiple sex partners for men (50% vs. 38%, p< .05) and sex trading for women (30% vs. 18%, p< .01). All reported significant decreases in frequency of unprotected sex, number of partners, and sex trade over time. Participants with sexual abuse histories had faster declines in unprotected sex, and those in the skills-building groups benefited more than controls. There were no treatment effects for number of partners or sex trade, and individuals with sexual abuse histories were more likely to engage in these behaviors at 6-month follow-up. Gender did not moderate effectiveness of treatment.
Conclusions: Skills-building group interventions aimed at reducing unprotected sex can be highly effective for both male and female substance abusers with sexual abuse histories. However, sex trading and multiple partnerships remained prevalent, and this group may benefit from additional gender-specific interventions to address these risk behaviors.
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THE SPIRIT OF COMMUNICATION: MOTIVATIONAL INTERVIEWING AND NATIVE AMERICAN TEACHINGS.

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Aims: To develop a training curriculum to introduce motivational interviewing as a communication style and to discuss the approach in relationship to Native American teachings.
Methods: A needs assessment conducted by key stakeholder interviews in 2009 found that although American Indian and Alaska Native (AI/AN) providers in the Upper Midwest region wanted to be trained in the use of Motivational Interviewing (MI), the MI training programs in which the providers had participated had not resulted in adoption of MI. In order to facilitate the adoption of MI by AI/AN substance abuse providers in the Upper Midwest, a committee was created to work with staff in the ATTC Home office to develop a training curriculum with specific focus on culturally-appropriate ways of communicating. Curriculum goals, format and content were selected by cultural consultants. Content for the curriculum, based on Motivational Interviewing Network of Trainers (MINT) discussions, was infused with AI/AN teachings. The curriculum was piloted with two groups, in Minnesota and South Dakota, with a total of 34 participants. Pilot participants were asked to complete a post-event survey evaluating satisfaction with the training and usefulness of information. While we had a 91% response rate, 14 participants were excluded from data analysis because they reported being of non-AI/AN background, for a final N of 19.
Results: A majority of participants (74%) reported being very satisfied with the training. Participants found the training useful (95%); expected to use information gained from the training (100%); and expected that information gained from the training would benefit their clients (100%). Accordingly, a first edition of a culturally-adapted training curriculum on MI for AI/AN Audiences was released in October 2012.
Conclusions: The Spirit of Communication training on Motivational Interviewing may be a promising means of providing culturally competent training to AI/AN treatment providers on the evidence based practice of Motivational Interviewing.
Financial Support: This study was completed by Prairielands ATTC under a cooperative agreement from SAMHSA.

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PRESCRIPTION OPIOID PATIENTS IN ADDICTIONS TREATMENT: CHARACTERISTICS AND CHALLENGES FOR TREATMENT PROVIDERS.

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Aims: Opioid use problems are growing at significant rates throughout the U.S., with alarming consequences. Overdose deaths have increased four-fold between 1999 and 2008 (CDC, 2011), driven in large part by increases in the non-medical use of prescription opioids (SAMHSA, 2012). A five-year period of admissions (N = 9,695) to a residential treatment center were assessed to compare the characteristics of prescription opioid patients to others.
Methods: Problems with multiple substances are common among addiction treatment samples. As such, the population was divided into groups based on primary drug of choice (DOC).
Results: The patient population with opioid dependence (excluding heroin) grew 57% between 2007 and 2011, mirroring national trends. Prescription opioid patients, specifically (n = 1,190), differed from those with alcohol or other drugs as DOC. These individuals were younger in age (M = 35, SD = 11.97) than cocaine (M = 37, SD = 9.48) or alcohol patients (M = 44, SD = 11.75), but older than marijuana patients (M = 31, SD = 10.12), $p < .001$. Groups did not differ on the number of co-occurring mental health diagnoses (M = 1.40). Opioid patients had significantly shorter lengths of stay (M = 25 days, SD = 7.85) compared to alcohol patients (M = 26, SD = 6.40), $t(1445) = -3.21$, $p = .001$, and were less likely to complete treatment (with a 16% atypical discharge rate) compared to the other groups, $X^2 = 133.63$, $p < .001$. Among opioid patients, females were overrepresented in atypical discharges. Compared to those whose primary DOC was alcohol, prescription opioid patients had lower self-efficacy at treatment entry, $t = -5.588$, $p < .001$.
Conclusions: Given the documented role of self-efficacy and treatment completion for favorable outcomes, these data suggest that specific evidence-based interventions are needed to improve chances for positive treatment outcomes.
Financial Support: Supported by private donations to the Butler Center for Research, Hazelden Foundation.

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MONITORING ALCOHOL ABUSE PREVENTION LEGISLATION.

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Aims: On July 1, 2011 Maryland (MD) increased its alcohol sales tax by 50%, from 6% to 9%. Some heralded the tax increase as an important step towards reducing underage drinking and alcohol abuse; others predicted that rather than lowering consumption, higher taxes would simply drive purchases across state lines into bordering states. Literature on cross-border effects of alcohol tax increases in the U.S. is very limited. We hypothesized that consumers proximal to state borders might cross state lines to make purchases, especially if those bordering states had lower tax rates than MD. This study explored changes in alcohol consumption related to this tax-based legislative prevention strategy.
Methods: We obtained sales data (county-level data in gallons of spirits, wine, and beer sold) for fiscal quarters pre- and post-tax rate increase, through December 31st, 2011. Geospatial methods and robust linear regression were used to explore several potential predictors of county-level changes in consumption.
Results: Post-tax increase, MD's statewide alcohol consumption patterns reflect those patterns seen at the national level: increasing spirits and wine sales and decreasing beer sales. However, when we examined alcohol consumption at the county-level we detected an on-average 5.4% decrease in spirits sales in MD counties bordering states with lower tax rates (β=5.4; CI: 2.1%, 8.7%; p=.008), but no change in beer or wine sales.
Conclusions: These preliminary results suggest that in MD, for counties bordering states with lower alcohol taxes, cross-border shopping for spirits may have occurred in the wake of the tax increase. However, due to increased sales elsewhere in the state, we found no detectable decrease in MD's alcohol consumption post-tax.
Financial Support: This work was supported by NIDA grant T32-DA007292 (PI: C. Debra Furr-Holden)

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WHY IS A DISCRIMINATION TEST IMPORTANT IN HUMAN ABUSE LIABILITY STUDIES?

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Aims: Demonstrate why Drug Discrimination is important
A Drug Discrimination Test is needed to screen for subjects that can discriminate between the class of drug being studied and placebo before being randomized to investigational treatment so that poor discriminators do not bias results.
Methods: The results of Drug Discrimination testing from two completed HAL studies that enrolled recreational users of opioids and used oral solutions that were similar in route, dosage, and strength of the active drug being investigated. Criteria for drug discrimination:
Drug Liking (bipolar VAS 0-100 point scale)
-a minimum score of 65 points for Drug Liking in response to active treatment at any time during the first 2 hours following dosing, and
-a ≥15-point difference between active and placebo treatments during the first 2 hours following dosing, and
-a placebo response ≥ 40 and ≤ 60 points for Drug Liking during the first 2 hours following dosing.
Drug High (unipolar VAS 0-100 point scale)
-a ≥30-point difference between active and placebo treatments during the first 2 hours following dosing, and
-a placebo response ≥ 0 and ≤ 10 points for Drug High during the first 2 hours following dosing.
Results: In these two studies, 156 subjects entered the drug discrimination test; 100 (64%) subjects passed discrimination; 39 (25%) subjects failed for inability to discriminate; 9 (6%) subjects failed for a positive placebo response; 7 (4%) subjects were unable to tolerate the active drug substance; 1 (1%) subject failed due to other reasons.
Conclusions: 25% of subjects failed discrimination for inability to discriminate between the active control and placebo. If poor discriminators are not excluded from the randomized treatment period of a HAL study, they could adversely affect study outcomes and prevent a clear separation between an investigational drug and active comparator.
Financial Support: This research is supported by CRI Lifetree from data obtained through Cephalon Inc. and King Pharmaceuticals, which was acquired by Pfizer Inc. in March 2011, sponsored studies.

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THE EFFECTS OF STRENGTH TRAINING ON COCAINE SELF-ADMINISTRATION.

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Aims: Previous studies have reported that voluntary wheel running decreases drug self-administration in laboratory rats, suggesting that aerobic exercise might be an effective intervention in substance abuse treatment programs. The purpose of the present study was to examine the effects of resistance exercise (i.e., strength training) on cocaine self-administration in rats responding on progressive ratio (PR) and fixed ratio (FR1) schedules of reinforcement.
Methods: Male, Long-Evans rats were obtained as young adults and assigned to exercising or sedentary conditions. Rats in the exercise condition climbed a 0.6-m ladder suspended 1.0 m above the floor while wearing a weighted harness. Rats in the sedentary condition were placed on top of the ladder without the weighted harness, thus receiving the same amount of handling and exposure to the climbing apparatus as the exercising rats. In Experiment 1, exercising rats performed one "superset" three days/week, performing 4-9 repetitions (i.e., climbs) and carrying up to 150 g above their body weight. In Experiment 2, exercising rats performed a three-set "pyramid" six days/week, performing 8, 6, and 4 repetitions and carrying up to their body weight.
Results: No differences were observed between exercising and sedentary rats on the PR schedule of reinforcement in either experiment. On the FR1 schedule, exercising rats self-administered less cocaine than sedentary rats when responding was maintained by a low dose of cocaine, and this effect was apparent in both experiments.
Conclusions: These data indicate that resistance exercise decreases responding maintained by a threshold dose of cocaine when response requirements are low. When these data are compared to data from previous studies in which rats engaged in voluntary wheel running, the magnitude of the strength training effect is small, suggesting that resistance exercise may be less effective than other forms of exercise at decreasing cocaine self-administration. These data provide limited support for the use of strength training interventions in substance abuse treatment programs.
Financial Support: NIDA grants R01DA031725 (MAS) and R01DA0274855 (MAS).

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THE INTERACTION BETWEEN SPOUSES' DRUG USE IN THE PREDICTION OF INTIMATE PARTNER VIOLENCE.

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Aims: Substance abuse at the individual level is a well-established risk factor for intimate partner violence (IPV). We know less of how the interaction between spouses' substance abuse relates to IPV. This study examined interactions between husbands' and wives' illicit drug use in the prediction of IPV frequency.
Methods: Data were analyzed from a community sample of newly married couples (surveyed at baseline and their 1st, 2nd, and 4th anniversaries; n = 538). Drug use was categorized into 3 groups: 1) no drug use, 2) marijuana use only, and 3) other illicit drug use (with or without marijuana use). Wives who used other illicit drugs were dropped from analyses due to insufficient sample size (n = 15). Our outcome variables were husband (H) to wife (W) and W to H IPV. We employed multivariate Poisson multilevel models, simultaneously examining both H and W IPV. We adjusted drug use estimates for sociodemographic variables, heavy alcohol use, and antisocial behavior.
Results: In a main effects-only model, H other drug use significantly predicted W to H IPV [incidence rate ratio (IRR) = 2.29; $p < 0.05$]. All other estimates for drug use were non-significant. Regarding H to W IPV, the interaction between H other drug use and W marijuana use was statistically significant ($p < 0.05$). The W marijuana use, H other drug use couples reported more frequent IPV than couples in which neither spouse used illicit drugs (IRR = 2.53; $p < 0.05$). H other drug use predicted greater frequency of W to H IPV regardless of W drug use (IRR = 4.61 if W used marijuana, IRR = 1.90 if W did not use drugs; $p < 0.05$).
Conclusions: These findings suggested that the interaction between spouses' illicit drug use was important when considering risk for IPV. Couples in which the husband used illicit drugs other than marijuana (with or without co-morbid marijuana use) and the wife used marijuana were at particularly heightened risk.
Financial Support: NIDA Dissertation Grant (1 R36 DA031996-01).

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LOCOMOTOR RESPONSE TO A NOVEL ENVIRONMENT: IDENTIFYING A USEFUL MEASURE OF INDIVIDUAL DIFFERENCES.

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Aims: A growing area of research on animal models focuses on baseline individual differences in behavior that can be used to predict vulnerability or resistance to drug abuse. One of the most popular measures of individual differences is locomotor response to a novel environment (LRNE), which was reported to be correlated with self-administration of cocaine, amphetamine, ethanol, morphine, and nicotine. However, it is unclear whether: (1) test parameters (e.g., test duration: 20 min vs. 2 hr) play a significant role in establishing individual differences; (2) curve fitting approaches describe locomotor response better than cumulative summaries (e.g., total activity); and (3) LRNE relates to other measures of response to novelty (e.g., novelty place preference, NPP).
Methods: The present study assessed these gaps by pooling data from four different studies using drug-naïve male Sprague-Dawley rats (N=270) in which rats experienced a 2-hr LRNE test.
Results: Distance traveled in the first 20 min of the test was very correlated with distance traveled across 2 hr ($r=.801$, $p<0.01$). Distance traveled is generally highest at the start of the session; total distance travelled during 2 hr therefore is heavily weighted by locomotor activity during the first few minutes. LRNE may best be characterized using growth curve modeling to describe the activity process over time. Preliminary analyses suggest that LRNE is well-described by polynomial and exponential functions. To determine the relation between LRNE and another measure of response to novelty, all rats were tested using the NPP test, and there was no correlation between proportion of time spent in the novel compartment and distance traveled over 2 hours ($p>0.05$), which suggests that these measures may reflect dissociable constructs.
Conclusions: Together, the results indicate that it is still unclear what trait the LRNE measures. Distance traveled is a cumulative measure that likely represents a time-dependent process and should potentially be modeled using curve fitting techniques.
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CLINICAL SUPERVISION OF DRUG COUNSELORS IN WUHAN, CHINA.

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Aims: To improve the provision of drug counseling during methadone maintenance treatment (MMT) in China, we developed and implemented structured initial training and ongoing clinical supervision procedures as part of a randomized clinical trial (RCT) of Behavioral Drug and HIV Risk Reduction Counseling (BDRC) and Educational Counseling (EC) in Wuhan, China
Methods: Training in BDRC and EC was provided to 8 counselors treating patients in the RCT (5 nurses, 2 counselors and 1 data clerk) and followed by weekly group clinical supervision sessions via Skype with supervisors in the U.S. Supervision sessions included case presentations by the counselors, discussion of the clinical interventions provided (or missed) during the counseling sessions, development of future session plans, as well as occasional re-training modules. We reviewed counselor attendance records and supervisory session review notes for the 39 supervision sessions held between November 2011 and 2012
Results: Counselors' participation in supervisory sessions averaged 81.5%. Common topics included specific and individualized interventions, techniques, and strategies to improve patients' daily medication adherence and regular attendance at counseling; educational strategies and skills to effectively increase patients' knowledge of treatment and HIV risks and prevention strategies; and interventions to help patients change their lifestyles and successfully manage the burdens of MMT treatment participation and the achieved lifestyle changes (e.g., daily MMT attendance while working full time). Supervisors utilized communication style and selected components of BDRC and EC (focus on positive consequences of behavioral change, behavioral contracts with counselors) to model and improve counseling skills of supervisees
Conclusions: Clinical supervision of drug counselors in MMT programs is feasible, accepted, and desired by the counselors; offers opportunities to improve professional skills and increases their adherence and competence in providing evidence based psychosocial interventions
Financial Support: NIDA DA026797 & CMHC/DMHAS/State of Connecticut

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PERFORMANCE OF SUBSTANCE USE DISORDER TREATMENT SYSTEMS: THE EFFECT OF CASE-MIX ADJUSTMENT.

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Aims: Transitional care between detoxification (detox) and rehabilitation in either residential or outpatient settings prevents detox readmissions and reduces patients' risk of death due to accidental overdose. As state agencies seek to evaluate local treatment systems on their performance with transitional care for detox patients, it is important to assess the effect of case-mix adjustment on performance outcomes.
Methods: Admissions data on all detox patients from 32 counties in California were abstracted from the California Outcomes Measurement System for 2008-2009 (N=24,928). Counties were ranked based on the proportion of detox patients transferred to any form of treatment within 14 days of discharge from a detox service. Case-mix adjusters were identified by examining their predictive power in a series of binary mixed models. Adjusted rankings were based on the mean predicted probability of a detox transfer for each county. A Kendall's tau coefficient was used to evaluate the impact of adjustment on county rankings.
Results: Important case-mix adjusters included Medi-Cal coverage, stable living situation, criminal justice referral to treatment, high school education, primary drug problem, prior treatment, lifetime mental illness diagnosis, and receipt of medication during treatment. The impact of case-mix adjustment on the county rankings was minimal (Kendall's tau=.9758), but it affected the relative rankings of 11 counties.
Conclusions: This study represents a first step in exploring the utility of case-mix adjustment for monitoring county-wide performance in transitional care for detox patients. Case-mix adjustment with CalOMS data has minimal impact on county rankings. Subsequent analyses will examine the role of county-level factors on transitional care performance such as county size, number of treatment programs, and funding levels.
Financial Support: Kirschstein-NRSA award (NIDA 5F31DA031509-01); State of California/Department of Alcohol and Drug Programs Evaluation Services to Enhance the Data Management System in California.

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INTERACTION OF GENDER AND GENETICS IN RESPONSE TO COCAINE VACCINE.

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Aims: To identify variants in genes associated with neurological physiology that differentially modulate response to cocaine vaccine treatment between male and female patients.
Methods: Sixty-six cocaine-dependent subjects were administered cocaine vaccine treatment or placebo via intramuscular injection at 0, 2, 4, 8 and 12 weeks, in tandem with behavioral cognitive therapy for both groups. Urine screening for a cocaine metabolite was performed thrice weekly, and change in number of positive urines was used to gauge treatment efficacy. DNA from participants was genotyped for the following genetic variants using Taqman assays (ABI): *GAD1* rs1978340 and rs769390, and *TPH1* rs1799913. Data was analyzed via repeated measure ANOVAs and was corrected for population structure.
Results: Analyses show that the genetic variants in *GAD1* (rs1978340 and rs769390), and *TPH1* (rs1799913) differentially mediate response to cocaine vaccine between males and females ($p \leq 0.0001$, $p \leq 0.0001$, and $p = 0.04$, respectively). Specifically, females carrying the A allele of rs1978340 in *GAD1*, males with the A allele of rs769390 and females with the C allele of rs769390 in *GAD1*, and men with the G allele in *TPH1* exhibited better response to the cocaine vaccine (e.g. fewer cocaine-positive urines) than those without these alleles.
Conclusions: These results illustrate that differences in genetic makeup and gender may modify the effectiveness of the cocaine vaccine in curbing cocaine use in cocaine-dependent (CD) individuals. This knowledge may help to tailor therapy for CD based on both genetic profile and gender, therefore increasing the probability of response to treatment.
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BUPRENORPHINE FOR INPATIENT MEDICALLY ASSISTED WITHDRAWAL IN PRESCRIPTION OPIOID AND HEROIN USERS.

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Aims: A flexible short-term buprenorphine dosing protocol was developed for inpatients undergoing medically-assisted withdrawal from opioids, largely replacing the previous protocol using clonidine. The objectives of this study were to evaluate its effectiveness and safety.
Methods: A retrospective chart review was conducted of patients admitted from January 2010 to May 2012 treated with buprenorphine for medically-assisted withdrawal from opioids.
Results: A total of 351 patients were included: mean age 37±11 years, 60% male, 60% single. Overall, the protocol resulted in a total buprenorphine mean dose of 64±39 mg given over 7±3 days, and was well tolerated. Mean COWS score prior to first dose was 14±4. First day mean dose was 8±4 mg, peak mean dose of 13±5 mg was reached on days 2 and 3, then tapered down (scheduled and prn), with 71% completing. Completers (n=241) and non-completers (n=96) were different in admission total daily morphine equivalents of prescription opioids (494±412 vs 721±899 mg, p=0.03) and buprenorphine dosing (total mean dose 73±35 vs 43±38 mg over 8±2 vs 4±3 days, p<0.001). Prescription opioid only users (n=291) and regular heroin users (n=60) were different in mean age (38±12 years vs 33±9 years, p<0.01) and rates of successful completion (73% vs 59%, p=0.02).
Conclusions: Buprenorphine for inpatient medically-assisted opioid withdrawal has been shown to be an effective treatment strategy over the past 3 years at the Centre for Addiction and Mental Health. The treatment has been used in primarily prescription opioid users, with lower success rates associated with higher daily prescription opioid use and those using heroin on a regular basis. Further research into these associations to optimize treatment success is warranted.
Financial Support: Centre for Addiction and Mental Health

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EXPLORING GENDER DIFFERENCES AMONG PEOPLE WHO INJECT DRUGS IN AUSTRALIA: FINDINGS FROM THE 2012 ILLICIT DRUG REPORTING SYSTEM.

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Aims: The Illicit Drug Reporting System (IDRS), conduced since 2000, monitors the price, purity, availability and use of illicit drugs annually in Australia. The IDRS focuses mainly on: heroin and other opioids, methamphetamines, cocaine and cannabis. The IDRS also looks at issues related to drug use, such as injecting risk behaviours and mental health problems. This presentation explores gender differences among a group of people who inject drugs interviewed for the IDRS in 2012.
Methods: The IDRS involves the collection and analysis of three data sources: (1) interviews with people who inject drugs, (2) interviews with experts who work with drug users such as treatment personnel and (3) existing databases on drug-related issues such as customs and overdose data.
Results: Over 900 people who inject drugs were interviewed for the IDRS in 2012. An analysis of the demographics found some differences. Males were significantly more likely than females to be single (64% vs 46%), heterosexual (94% vs 82%) and have a prison history (63% vs 40%), while females were more likely to be in current drug treatment (50% vs 40%). Significant differences were also found between gender and recent drug use. Females were more likely to report the recent use of methadone (51% vs 43%), prescribed benzodiazepines (not including alprazolam; 40% vs 33%) and over the counter codeine (21% vs 12%). While males were more likely to inject prescribed buprenorphine-naloxone tablets (4% vs 1%) in the last six months. Information on gender differences associated with harms, risk behaviours and mental health were also noted.
Conclusions: Females among this group of people who inject drugs appear to be more engaged in drug treatment than their male counterparts. Yet, they were also more likely to be engaged in risky injecting practices and self-report mental health problems. Further work around appropriate harm reduction messages for women is required. Strategies to encourage males among this population to engage in treatment are also required.
Financial Support: National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia

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BRIDGING FROM CONVENTIONAL MARKETED IMMEDIATE RELEASE FORMULATIONS TO NEW TAMPER-RESISTANT ALTERNATIVES.

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Aims: Many solid immediate release (IR) dosage forms containing opioids can be abused by snorting of crushed product or preparation of solutions for subsequent injection. Tamper resistant IR formulations (TRF-IR) aim to prevent intentional abuse by crushing and dissolving. Gruenenthal (GRT) has developed a TRF technology (INTAC®) for extended release formulations, already available as marketed products. The technology has now been expanded for IR formulations also using a high molecular weight polymer as excipient. A switch from a conventional immediate release formulation to TRF product alternatives generally requires bridging bioequivalence studies.
The aim was to evaluate the relative bioavailability of a GRT-TRF-IR formulation (Test) of an analgesic in comparison to the marketed IR reference product of the same drug. The main pharmacokinetic target parameters were AUC(0-t) and Cmax.
Methods: This was an open-label, randomized, cross-over, relative bioavailability trial comparing Test against the reference product. Single oral doses were administered to healthy male subjects under fasted conditions. Serum drug concentrations were determined by a validated LC-MS/MS method. Non-compartmental PK analysis was performed and the usual 80.00 - 125.00% confidence interval acceptance criteria for bioequivalence were used for comparing Test to the reference.
Results: The 90% confidence intervals for Cmax and AUC(0-t) of Test were 89.74 - 117.32% and 94.24 - 109.97%, respectively.
The data demonstrate that GRT-TRF-IR tablets have comparable in-vivo performance to standard immediate release formulations.
Conclusions: TRF-IR tablets may enable physicians to simply switch patients from conventional to reformulated TRF products.
Financial Support: Gruenenthal GmbH, Aachen, Germany

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PROFILE OF SUBSTANCE USE RISK BY RACE AND RURALITY AMONG RE-ENTERING OFFENDERS.

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Aims: The ASSIST was developed and tested to detect substance abuse risk in health care settings. The NIDA-modified ASSIST is useful for targeting interventions because scores can map risk levels to indicators for brief intervention. However, the ASSIST has not been widely used in other settings such as criminal justice. This study utilizes the ASSIST, along with another tools for substance using offenders, to profile risk among prisoners preparing for re-entry to urban and rural communities by racial group.
Methods: The ASSIST and TCU Drug Screen were administered to 409 prisoners preparing for parole to urban and rural areas of Kentucky. Participants consented for data collection as part of the Criminal Justice Drug Abuse Treatment Studies (2) cooperative. Analysis of variance (ANOVAs) were conducted to examine substance use risk by race (white/non-white) and rurality (urban/rural), as well as the potential interaction.
Results: A main effect of race was found for several ASSIST drug scores with white offenders scoring higher in each use category including stimulants ($p<.05$), methamphetamines ($p<.000$), sedatives ($p<.01$), street opioids ($p<.05$), prescription opioids ($p<.000$). In addition, a main effect of race was also observed for the TCU Drug Screen ($p<.000$). In addition, whites were more likely to meet the criteria for substance use dependence ($B=1.1$, $OR=0.35$, $p<.000$). There were no main effects for rurality, and no interactions between race and rurality in any of the models
Conclusions: While tools like the TCU drug screen may predict substance abuse problems, the ASSIST may detect specificity for risk across certain categories of drugs, as well as risks by subgroups of offenders – such as those in racial groups. Through CJDATS2, state DOC systems worked through change teams to improve the assessment process, which may include increased utilization of more standardized tools such as the ASSIST.
Financial Support: CJ-DATS is funded by NIH/NIDA in collaboration with SAMHSA and DOJ.

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SUBSTANCE USE AND SEXUAL BEHAVIOR AMONG WOMEN IN PRAGUE.

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Aims: In the 1980's, the Czech Republic was protected from the first waves of HIV transmission by socialism and travel restrictions. Now, HIV incidence in the Czech Republic approaches that of Western Europe a decade ago. Women without obvious risk factors are being identified as HIV positive. Our aim was to explore substance use and sexual practices of women who frequented selected social venues in Central Prague.
Methods: A cross-sectional survey collected characteristics about a female subset (n=124) from a larger sample (N=377) of heterosexual and gay & lesbian young adults aged 18 and over; tourists and those unable to speak Czech were excluded. We assessed patterns of drug use including the CAGE screen, sexual behaviors, and HIV testing and knowledge. Statistical analysis consisted of central tendency, chi-square, ANOVA, and multiple regression models.
Results: Respondents were 18 to 67 years of age, mean 29 years; 85% were Czech, 8% Slovak, 2% Roma, and 5% other; 25% self-identified as non-heterosexual (homosexual, bisexual, or female-to-male transgender). Alcohol was their drug of choice; 10% reported excessive use. Young unmarried women with new, multiple sexual partners within the last six months had a positive association ($p>0.04$) for high use; a significant negative association ($p>0.000$) to high use was noted among unmarried women with children. Only 18% of the women reported consistent condom or oral barrier use; 60% never used condoms, associated with unmarried status, multiple male partners, and short duration of relationship ($p>0.002$). HIV testing was reported by 32% and was associated with younger age and knowledge of pre-/post-exposure prophylaxis ($p<0.04$). Half of the women expressed willingness to use pre-/post-exposure prophylaxis if available.
Conclusions: Reported alcohol excess and sexual practices by this sample describe sexual behavioral and addiction risk regardless of sexual identity. To maintain low levels of HIV transmission, updated health messages regarding safer sex and drug use behaviors are recommended.
Financial Support: This presentation is funded by NIH/NIDA T32 DA026400, Training Program on Addiction Medicine in Primary Care.

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COPING STYLE AND SERVICE UTILIZATION AMONG AFRICAN-AMERICAN FEMALE DRUG UERS.

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Aims: According to the National Survey on Drug Use and Health, African Americans' past month illicit drug use and treatment need exceeds the national average (SAMHSA, 2012). The purpose of this study is to explore coping style and individual factors related to treatment among African American female drug users.
Methods: Data were derived from 105 African American female drug users. Bivariate correlations were conducted, followed by a logistic regression. Participants were asked "Have you ever participated in a drug or alcohol treatment program?" with 38% of the women responding "yes." The independent variables of interest were age, education, motherhood, partner status and the John Henryism Active Coping (JHAC). It was hypothesized that women who were older, more educated, were mothers, and employed more active coping would be more likely to have ever participated in treatment.
Results: The model was significant ($\chi 2$ (4) = 35.99, $p < .001$). For every year increase in age the women were more likely to have participated in drug or alcohol treatment (OR = 1.07, $p < .01$). For every one unit increase in education level, women were 31% less likely to have participated in drug or alcohol treatment (OR = .69, $p < .01$). For every one unit increase in active coping, women were 14% less likely to have participated in a drug or alcohol treatment program.
Conclusions: The study adds to the literature that drug using African American women with a higher education level and who report higher levels of active coping are less likely to have ever participated in a drug or alcohol treatment program. It may be that higher educated African American women who utilize active coping strategies to manage daily stressor may perceive less treatment need. The study is limited in that it is unable to predict drug use as a result of active coping over time. Future studies are needed to examine perceptions of higher educated African American women with regard to their drug use patterns and active coping.
Financial Support: NIDA R01-DA2297; PI, Oser and NIDA K08-DA32296; PI Stevens-Watkins

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METABOTROPIC GLUTAMATE RECEPTOR 7 ACTIVATION WITH AMN082 ATTENUATES THE REINFORCING AND MOTIVATIONAL EFFECTS OF NICOTINE IN RATS.

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Aims: Accumulating evidence indicates that activation of the metabotropic glutamate receptor 7 (mGluR7) inhibits the rewarding effects of drugs of abuse, such as cocaine and alcohol. mGluR7s are presynaptically located and negatively modulate glutamatergic neurotransmission in various brain sites, including the dorsal striatum (CPu), and ventral tegmental area (VTA). The present study assessed mGluR7 involvement in nicotine dependence.
Methods: The effects of mGluR7 activation with N,N'-dibenzhydrylethane-1,2-diamine dihydrochloride (AMN082) on the reinforcing and motivational aspects of nicotine dependence were evaluated using the intravenous nicotine self-administration procedure in rats. AMN082 was administered systemically, and centrally into the VTA and CPu to determine the loci of action.
Results: Intraperitoneal administration of AMN082 (0, 3, 10 and 20 mg/kg) significantly attenuated nicotine self-administration under fixed (FR) and progressive ratio (PR) schedules of reinforcement, indicating that activation of mGluR7 attenuated both the primary reinforcing and incentive motivational effects of nicotine. Central injections of AMN082 (0, 1, 3 and 5 μg/side) into the VTA, but not the CPu, decreased nicotine self-administration under an FR schedule of reinforcement; suggesting involvement for the VTA, but not CPu, in the effects of AMN082 on nicotine dependence.
Conclusions: Activation of mGluR7 attenuates nicotine self-administration in rats through a neural circuitry involving the VTA, but not the CPu. The attenuation of nicotine self-administration resulting from pharmacological activation of mGluR7s in the VTA is presumably mediated by inhibition of glutamate efflux from the VTA leading to a decrease of firing activity of dopaminergic projections from the VTA to the NAc, a pathway critically involved in the reinforcing and motivational effects of nicotine. Together, these findings suggest therapeutic value of mGluR7 activation in the treatment of nicotine dependence.
Financial Support: TRDRP Postdoctoral Fellowship 21FT-0022 to AKS and TRDRP New Investigator Award 20KT-0046 to XL

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CRACK-COCAINE USERS SHOW DIFFERENCES IN GENOTYPE FREQUENCIES OF THE DOPAMINE TRANSPORTER GENE (DAT1/SLC6A3) 3'UTR VARIABLE NUMBER OF TANDEM REPEATS.

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Aims: To compare the prevalence of allele and genotype frequencies created by the 3'UTR VNTR at DAT1 gene between adult CCU and controls. Due to its mechanism of action on drug addiction, this gene can be a good candidate for molecular studies.
Methods: A cross-sectional sample of 237 current adult crack abusers or dependents (DSM-IV TR criteria) from in- and outpatient clinics and 211 community non-CCU (controls) were collected in southern Brazil. Subjects were evaluated with ASRS, ASI6 and MINI-Short. IQ was estimated using WAIS. DNA samples extracted from whole blood were genotyped for the DAT1 3' VNTR. A hypothesis of association was investigated using Chi-square and Logistic regression tests.
Results: The 10-repeat allele and 10.10 genotype were the most prevalent in cases (74.1% e 59.9%, respectively) and controls (68.2% and 48.8%, respectively). A paired analysis considering 10.10 (putatively the risk genotype) versus other genotypes showed a higher, though not significant, prevalence of 10.10 homozygous in cases versus controls (54.5% versus 45.5%; Mcnemar p=0.059; 190 pairs regarding sex, age and ethnic group). The non-paired analyzes including all the 448 subjects showed a statistically significant difference (58% versus 42%; Pearson Chi-square p=0.018), that remained after controlling by sex, age and ethnic group (Logistic Regression p=0.010).
Conclusions: This is one of the first genetic association studies with CCU in the literature, suggesting an influence of the DAT1 gene, namely the 3' VNTR 10.10 genotype, in crack-cocaine dependence. This result corroborates the role of DAT protein in neurobiology of drug addiction. However, more analyses must be performed with this and other DAT1 polymorphisms, to confirm and clarify its contribution as a possible risk factor for crack-cocaine dependence.
Financial Support: SENAD, FAPERGS, CNPq, CAPES, PRODAH

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ABUSE POTENTIAL OF TAPENTADOL COMPARED TO TRAMADOL AND HYDROMORPHONE IN RECREATIONAL OPIOID USERS.

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Aims: Tapentadol is a novel analgesic that activates mu opioid receptors and blocks norepinephrine reuptake. There is very little information available regarding the abuse potential of tapentadol. This study evaluated the physiological, subject-rated and performance effects of tapentadol compared to two control drugs in humans. We hypothesized that all three drugs would produce comparable prototypic mu opioid effects (e.g., miosis, increased ratings of "Like the Drug"), but that tramadol also would produce negative effects (e.g., increased ratings of "Bad Effects").
Methods: This outpatient, double-blind, within-subject study examined the effects of oral placebo, tapentadol (25, 50 and 75 mg), tramadol (50, 100 and 150 mg) and hydromorphone (2, 4 and 6 mg). Nine human recreational opioid users completed the study. Drug effects were measured before and for 6 hr after drug administration. Data were analyzed with repeated measures ANOVA.
Results: All three doses of the tested drugs produced comparable, time-dependent decreases in pupil diameter, but the effects were generally not dose-related. The high dose of tapentadol, as well as all three doses of tramadol and hydromorphone, increased positive subject-rated effects (e.g., "Good Effects," "Like the Drug") as a function of time. Only tramadol increased negative subject-rated effects (e.g., "Bad Effects," "Nauseous").
Conclusions: The highest tested dose of tapentadol produced a profile of positive effects comparable to those of hydromorphone, whereas tramadol produced positive and negative subject-rated effects. These data suggest that tapentadol has significant abuse potential, at least on the level of hydromorphone. The mixed subject-rated profile of tramadol is consistent with previous findings indicating reduced abuse potential relative to the prototypic opioids.
Financial Support: Grant R01 DA 025649 (PI: WWS) and Departmental Startup Funds awarded to WWS.

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RELATIONS BETWEEN CRAVING AND WITHDRAWAL AND TIME TO FIRST OPIOID USE AMONG PRESCRIPTION OPIOID ABUSERS INITIATING BUPRENORPHINE DETOXIFICATION.

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Aims: To quantify the relations between craving and withdrawal symptoms and time to first opioid use among prescription opioid (PO) abusers undergoing buprenorphine detoxification. Higher indicators of craving and withdrawal at the outset of the taper were hypothesized to predict earlier use.
Methods: Data from 653 PO-dependent individuals initiating a 14-day taper from Buprenorphine/Naloxone, recruited for the CTN POATS study, were analyzed using survival analysis to explore time to first use as a function of opioid craving and withdrawal. Participants were collapsed across condition and measurements taken at the start of the taper were used. Participants were followed for 10 weeks after the taper began. PO craving was measured by 3 items on the Visual Analog Scale (VAS; e.g., "How much do you currently crave opiates?") and opioid withdrawal was measured by the Clinical Opiate Withdrawal Scale and 1 item on the VAS.
Results: Withdrawal significantly predicted time to first use (X2=4.17, p=.04), such that each withdrawal unit increase led to a 1.0% decrease in time to first use. Craving items significantly predicted time to first use (X2=17.3-22.2, p<.0001). Each unit increase on the craving item response scales was associated with a 1.7% to 1.9% decrease in time to first use, depending on the item. Further analyses revealed differences among individuals who terminated study involvement after the first taper and those willing to take part in a second taper.
Conclusions: Higher reports of withdrawal and craving at the outset of a buprenorphine taper are important clinical indicators of earlier lapse to opioids. Novel therapies to attenuate these effects are needed.
Financial Support: This project was supported by the NIDA Clinical Trials Network (NCT00316277).

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ADVANCED METHODS FOR CAUSAL INFERENCE IN DRUG ABUSE OBSERVATIONAL DATA.

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Aims: Establishing causal linkages between variables in naturalistic studies is difficult both for conceptual and practical reasons. However, methods for data capture from prospective longitudinal studies of psychiatric disorders, in combination with recently-developed statistical methods, make it less difficult to disentangle causal sequences. The purpose of this presentation is to describe these methods and their application to a study of social connections in drug abuse.
Methods: A new naturalistic study of outpatient drug abuse clients will examine the time-varying effects of social connections on substance use and HIV risk behaviors, and vice versa. Prior research has shown strong and long-lasting effects of social connections, but only limited data on why drug abusers make good vs. bad social connections. The study will combine time-line methods for substance use with methods for intensive longitudinal data capture adapted from psychiatry studies to gain a comprehensive picture of social and behavioral changes over two years post-treatment. An instrument to determine a time-line for social changes has been developed. Statistical methods that use lagged time-varying predictors to analyze event history or continuous outcomes help to establish temporal precedence, which as Kazdin and Nock have noted is crucial for inferring causality. Propensity matching methods will also be used where feasible to bolster causal inferences.
Conclusions: Since many important drug abuse research questions, such as the reciprocal impact of social links on substance abuse, can only be addressed by naturalistic research, recent methodological improvements for such studies are important for the field. The new study will provide an example of how intensive longitudinal data in conjunction with advanced statistical methods can provide new information about the determinants of drug abuse.
Financial Support: NIDA grants R21 DA026541 and R01 DA031154.

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PREDICTORS OF INJECTION CESSATION AND RELAPSE AMONG FEMALE SEX WORKERS WHO INJECT DRUGS IN TWO MEXICAN-U.S. BORDER CITIES.

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Aims: To identify predictors of injection cessation and relapse among FSW-IDUs in Tijuana and Cd Juarez.
Methods: Participants were HIV-negative FSW-IDUs >18 years at baseline who reported sharing injection equipment and unprotected sex with clients within the last month. Women participated in a randomized factorial trial aimed at promoting safer sex in the context of drug use and safer injection behaviors, and underwent quarterly interviews and testing for HIV and STIs for 12 months. Cox regression was used to predict time to first cessation of injection, and given cessation, time to injection relapse, controlling for intervention assignment.
Results: Of 440 initially HIV-negative FSW-IDUs, 97% injected heroin. Only 12% had ever received methadone maintenance (MMT); 84 (19%) women reported ceasing injection (median time to cessation: 9.3 months) among whom 30 (35%) reported relapse to injection (median time to relapse: 3.5 months). In multivariate Cox models, time to first injection cessation was longer for women who reported: first trading sex prior to age 18, ever being sexually abused, and more vaginal sex acts with casual clients. Time to injection cessation was shorter for women in Tijuana vs. Cd. Juarez and those spending more time on the streets. Time to relapse was shorter among women who reported: lower incomes, regularly using drugs with clients, and those with higher risk injection behaviors. Neither intervention assignment nor MMT was associated with cessation or relapse.
Conclusions: FSW-IDUs face unique structural barriers related to both sex work and drug use that necessitate additional supports to support their attempts to stop injecting drugs. These findings have salient implications for programming in Mexico as the country is scaling-up access to MMT.
Financial Support: R01DA023877

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ATTITUDES TOWARD AND PREFERENCES FOR HEALTH RESEARCH AMONG DRUG USERS AND NON-DRUG USERS.

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Aims: The clinical and translational research enterprise requires the participation of the population in health research, yet less than 1% actually participates in clinical trials. Effective strategies to increase research participation are needed; drug using populations are especially vulnerable to underrepresentation due to medical and non-medical ineligibility. The Transformative Approach to Reduce Disparities Towards Drug Users (R01DA027851: Cottler, LB, PI) is a NIDA CTSA randomized trial; it assesses effectiveness of an ambassador model compared to none when enrolling drug using and non-drug using participants in relevant research, and in referring participants to medical care and other needed services. In this comparison of a matched sample of drug users and non-drug users, we compare attitudes toward and preferences for health research.
Methods: For this comparison, a random race-matched sample of adult drug users (n=80) and non-drug users (n=80) was used. Age was normally distributed. Data were obtained from the baseline assessment and analyzed with SAS 9.3.
Results: Drug users and non-drug users did not vary in most of their attitudes towards research. However, drug users were less likely than non-drug users (37% vs, 63%, p=.011) to agree with the statement "research studies provide opportunities for care or treatment that I couldn't get any other way" and more likely to agree that research would give them something to do (48% vs. 43%; p=0.0576).
Conclusions: This comparison of attitudes and preferences among drug users and non-users could help catalyze a discussion on including drug users as research participants. Drug users attitudes towards research are generally no different than non-drug users, and their reasons for participation are the same, or where different, do not increase their vulnerability for coercion.
Financial Support: Transformative Approach to Reduce Disparities Towards Drug Users R01DA027951and Supplement-05S1

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AMYGDALA FUNCTIONAL CONNECTIVITY DURING CRAVING INHIBITION ATTEMPTS AT BASELINE PREDICTS CRAVING AND COCAINE USE.

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Aims: Cocaine-dependent (CD) patients who submit cocaine-free urine status during a pre-screening period, a phenotype associated with better drug use outcomes, evidenced stronger functional connectivity between amygdala (AMYG) and frontal modulatory regions when attempting to inhibit cocaine craving (CPDD, 2010). In a prospective study, we used an "attempted inhibition of craving" paradigm to test whether 1) greater fronto-limbic connectivity would predict less craving and drug use, while 2) greater AMYG intra-limbic connectivity would be linked to increased craving and drug use.
Methods: Thirteen CD patients were scanned after 7 days in a controlled therapeutic setting to ensure stable, cocaine-free state. We used block-design BOLD fMRI to measure brain response and subjective craving under the following 3 conditions: 1) neutral video; 2) cocaine video; and 3) cocaine video while attempting to inhibit craving (INHIBIT). Data were analyzed within SPM8, using functional connectivity analyses with AMYG as the reference region. Percentage of cocaine-positive urines were assessed as outcome measure.
Results: During INHIBIT, greater AMYG intra-limbic functional connectivity was associated with greater craving level during INHIBIT ($r=0.699$, $p<0.01$). There was a significant level of AMYG connectivity in subgenual extending to supragenual cingulate associated with more frequent cocaine use ($r=0.699$, $p<0.01$).
Conclusions: Strong intra-limbic connectivity during modulatory attempts to inhibit craving predicted high craving level. Functional connectivity between subgenual cingulate and AMYG predicted higher frequency of cocaine use. These functional markers may represent important phenotypic biomarkers and a potentially valuable treatment target.
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BUPRENORPHINE/NALOXONE FOR THE TREATMENT OF PRESCRIPTION OPIOID ABUSE AND CHRONIC PAIN.

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Aims: The incidence of prescription opioid abuse among pain patients is substantial, and the ability of sublingual buprenorphine simultaneously to alleviate pain and reduce opioid abuse has not been investigated adequately. This study examined the utility of buprenorphine/naloxone (bup/nx; Suboxone) for treating patients diagnosed with concurrent chronic pain and opioid abuse.
Methods: Participants with chronic, non-malignant pain meeting DSM-IV criteria for opioid abuse enrolled in a 7-week inpatient phase examining the effects of bup/nx on the reinforcing effects of prescription opioids. Those who completed this phase were subsequently enrolled in an 12-week outpatient trial designed to examine the safety, tolerability, and efficacy of bup/nx in relieving clinical pain. Participants attended twice-weekly visits, completed pain ratings, and met with the study physician. The bup/nx dose was titrated to optimal clinical benefit. Primary outcomes were retention in treatment, pain reduction from pre-study baseline, and percentage of opioid-negative urine samples.
Results: The majority of patients (31/43; 72.1%) inducted onto bup/nx completed the inpatient phase and were enrolled in the present trial. Further, the majority (18/31; 58.1%) of patients who began the 12-week outpatient phase were retained at study completion. Mean ratings of average pain on the Pain Assessment and Documentation Tool (PADT) decreased significantly from 6.2/11 (+/- 1.2) at pre-study baseline to 3.6 (+/- 2.5; $t(17)=4.17$, $p=.001$) at Week 12. The mean daily dose of bup/nx at Wk 1 was 15.8 mg (+/- 2.3, range 4-20) and at Wk 12 was 21.3 mg (+/- 7.8, range 4-32). The percentage of urine toxicologies negative for illicit opioids increased from 6.4% at baseline to 88.5% at Wk 1, 90% at Wk 4, and 93.4% at Wk 12.
Conclusions: Bup/nx was well tolerated and effective in preventing relapse to prescription opioid abuse while providing adequate analgesic relief. Sublingual bup/nx has potential as an analgesic and may be well suited to treating patients with chronic pain who abuse opioids.
Financial Support: NIDA RO1 DA20448

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THE EFFECT OF TOBACCO USE ON BRAIN PHOSPHOCREATINE LEVELS IN FEMALE METHAMPHETAMINE USERS.

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Aims: Methamphetamine (MA) use is associated with altered cerebral metabolism, including reduced levels of the high energy buffer compound phosophocreatine (PCr, Sung 2012). Although tobacco smoking (TS) is common among MA users, its impact on brain high energy phosphorus metabolites is not well understood. Importantly, TS has been associated with a reduced incidence of Parkinson's disease, and long-lasting MA effects on nigral-striatal dopamine neurons mimic the neurodegenerative process of Parkinson's disease. Thus, we hypothesize that lifetime TS will have a significant positive correlation with brain PCr levels in MA users, indicative of improved brain cerebral metabolism.
Methods: Phosphorus-31 magnetic resonance spectroscopy evaluated 21 female (age 30±7 yrs) and 24 male (age 35±6 yrs) MA users. A chemical shift imaging free induction decay pulse sequence was used to investigate PCr levels in the bilateral frontal lobe voxels with TR/TE=3000/2.3ms, matrix=8×8, FOV=20×20cm2, slice thickness=2.5cm.
Results: We found a significant positive relationship between brain PCr levels and lifetime TS in female MA users (p=.02) but not in male users (p=.81). In addition, significant interactions between lifetime MA use and lifetime TS were seen only in female MA users (p=.01). These findings suggest that lifetime TS may have a more significant impact on brain PCr levels in heavy than light female MA users.
Conclusions: These preliminary results are consistent with reports of neuroprotective effects of nicotine on Parkinson's disease as well as an attenuation of MA-induced neurodegeneration by nicotine pretreatment in wild-type mice (Pauly 2004). The effects of TS on PCr levels seem to be gender-specific. Since there is evidence that smoking cessation is related to depression in women, the association of PCr levels with TS might be related to the higher incidence of depression in female MA users. Further investigation is required to characterize the relationship between the altered PCr levels by nicotine use and psychiatric symptom changes.
Financial Support: 1R01DA027135

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ADDICTION AND CONTINUOUS HIV CARE FOR INDIVIDUALS WITH A HISTORY OF INCARCERATION.

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Aims: The high prevalence of HIV among incarcerated populations has led practitioners and researchers to view correctional institutions as necessary places to intervene with public health efforts. This study utilizes a biopsychosocial model to explore the barriers and facilitators to continuous HIV care for individuals with a history of incarceration.
Methods: Data comes from 30 in-depth interviews with formerly incarcerated individuals living with HIV in Delaware, and a focus group with staff at a local community HIV clinic.
Results: The findings presented in this paper reveal the processes by which addiction is an especially prominent barrier to continued HIV care upon release from incarceration. The majority of the participants in this study experienced HIV treatment interruption as a result of relapse to addiction once they were released from incarceration. Once individuals relapsed, a number of factors contributed to HIV treatment interruption, including re-incarceration, a lack of concern for HIV care, and the overlap of symptoms between addiction and HIV infection. Conversely, linkage to and retention in HIV treatment was facilitated by the cessation of substance abuse for the majority of the study participants.
Conclusions: Relapse to addiction was a primary barrier to continued HIV care once individuals were back in the community after incarceration. In addition, individuals were more likely to engage in HIV treatment when they were no longer using substances. Thus, it is critical to include linkage to addiction treatment providers in reentry discharge planning. Integrated case-management should continue once the individual is released to the community to ensure treatment needs continue to be met in order to facilitate continued HIV care. Pre-release assistance with housing could also reduce the chances of returning to the 'people, places, and things' that foster relapse to addiction.
Financial Support: This research was supported by the National Institute On Drug Abuse of the National Institutes of Health under Award Number F31DA031510. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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IBUDILAST MAY REDUCE INATTENTION ASSOCIATED WITH METHAMPHETAMINE USE.

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Aims: Inattention is the most reliable and robust deficit related to methamphetamine (MA) abuse. We sought to determine if Ibudilast (IB) might reduce the impact of acute MA exposure on attention in contrast to a placebo.
Methods: This study was conducted within an IB safety-interaction trial. Participants (n=8) were fluent in English, dependent on MA only, and free of neurological and non-MA related psychiatric disorders. Participants completed assessments at baseline, where they were MA negative and pre-study medication exposure, and prior to discharge, where they were on IB (100 mg; n=4) or placebo (P; n=4) 48hrs after exposure to MA (30 mg IV). The assessments included the Conners' Continuous Performance Test-II (CPT-II), a test of attention. Group differences in CPT-II performances were determined by Mann-Whitney U tests. The groups were similar in education (U=3.50, p=.18), but differed in age (U=1.00, p=.04, r=-.72), so we utilized demographically corrected T-scores for CPT-II comparisons. We restricted analyses of the CPT-II to six indices that were deficit in our sample's baseline assessment.
Results: The groups were similar on their baseline CPT-II performances (Us=4.00-7.00, ps=.25-.77). At follow-up, however, the IB group showed reduced variability in response times (U=0.00, p=.02, r=-.82) and perseverative responses (U=1.50, p=.04, r=-.71) in contrast to the P group. No other differences between groups on CPT II performance were detected (Us=3.00-4.50, ps=.20-.34).
Conclusions: Our results suggest that high dose IB may have a protective effect on attention in the face of early MA abstinence. While it is unclear whether these differences were due to improved attention, these results suggest that IB may help to improve cognitive function in early MA withdrawal. Data provide some support for developing MA treatments that reduce cognitive impairment.
Financial Support: Financial Support: National Institute on Drug Abuse (1R01DA029804; S. Shoptaw); National Center for Advancing Translational Sciences (UL1TR000124; S. Dubinett).

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A SYSTEMATIC REVIEW OF STUDIES EXPLORING CRAVING, ITS MODERATORS, AND THE LINK WITH SUBSTANCE USE IN DAILY LIFE USING ECOLOGICAL MOMENTARY ASSESSMENT (EMA).

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Aims: Studies examining the link between craving and substance use have often revealed contradictory results. Ecological Momentary Assessment (EMA) is a method particularly well-suited to assess subjective variables and episodic events in daily life, and it offers a new opportunity to examine questions concerning craving with high ecological validity. The objective of this systematic review was to examine all published studies using EMA to: 1) examine the temporal link between craving and substance use, and 2) identify relevant moderators of craving intensity among substance users.
Methods: The literature search used Medline up to July 31, 2012, and was based on a systematic review methodology.
Results: Fifty-seven studies were selected, of which most concerned tobacco or alcohol. The majority of studies (91%) reported a positive relationship between craving and substance use, both concurrently and prospectively, within pre- and post-quit periods, among users with different levels of use, and for both legal and illegal substances. EMA data also confirmed the influence of intra-individual variables (negative affects, social contexts, other substance use) and inter-individual variables (age, level of use) in daily life craving reports
Conclusions: This review of EMA investigations demonstrates a strong link between craving and substance use, and underscores the importance of taking into account temporal and contextual considerations in the assessment of this relationship.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008, CNRS ATIP

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LOWER SEROTONIN 2C RECEPTOR (5-HT2CR) EXPRESSION IN THE VENTRAL TEGMENTAL AREA (VTA) ASSOCIATES WITH ELEVATED CUE REACTIVITY FOLLOWING EXTENDED FORCED ABSTINENCE FROM COCAINE-TAKING.

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Aims: Vulnerability to environmental cues previously associated with cocaine-taking ("cue reactivity") is thought to promote relapse. The VTA has been implicated in cue reactivity such that exposure to cocaine-associated cues has been shown to trigger activation of the VTA in neuroimaging studies of cocaine-dependent subjects. The VTA microcircuitry and afferents that control cue reactivity are underexplored. Serotonergic afferents to the VTA may regulate cue reactivity through metabotropic 5-HT2CRs that exert an overall inhibitory impact over VTA function. Impaired neuronal signal transduction in the VTA through the ERK1/2 pathway may contribute to adaptations underlying responses to cues; however, altered 5-HT2CR expression and signaling as a neurobiological driver of such events underlying cue reactivity is unknown. We tested the hypothesis that extended periods of forced abstinence (FA) from cocaine-taking results in elevated cue reactivity and shifts in the subcellular expression of the 5-HT2CR and pERK1/2.
Methods: Rats (n=20) underwent cocaine self-administration followed by 1 or 30 days of FA. Cue reactivity (presses on cocaine-conditioned lever) was measured on FA Day 1 or 30. Rats were sacrificed and VTA harvested. Immunoblotting was performed to assess VTA subcellular localization (membrane, cytosolic, nuclear) of 5-HT2CR and pERK1/2 protein.
Results: Cocaine-conditioned lever presses were elevated at FA Day 30 vs. FA Day 1 ($p<0.05$). Expression of membrane 5-HT2CR was lower while nuclear pERK1/2 was higher in the VTA on FA Day 30 vs. FA Day 1 ($p<0.05$). Cytosolic levels of pERK1/2 did not differ on FA Day 1 vs. FA Day 30.
Conclusions: Collectively, these data suggest reduced VTA 5-HT2CR expression concomitant with altered pERK1/2 nuclear translocation emerges during prolonged FA from cocaine SA to drive cue reactivity. Future directions will assess the impact of an imbalance in 5-HT2CR homeostasis as a driver of dynamic neurobiological events underlying cocaine cue reactivity.
Financial Support: DA07287, DA06511, DA024157

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SERUM CONCENTRATIONS OF BDNF DURING THE IMMEDIATE PUERPERIUM AMONG WOMEN WITH CRACK DEPENDENCE IN COMPARISON TO HEALTHY MOTHERS: PRELIMINARY DATA.

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Aims: The use of crack probably is experimented by the organism as something toxic, activating protective responses, like those mediated by Brain-Derived Neurotrophic Factor (BDNF). During pregnancy there are changes in immune system, such as in stress response, and some psychiatric disorders change their profile during or after pregnancy. The goal of this study was to compare serum levels of BDNF during the immediate puerperium among women with crack use vs healthy mothers
Methods: Study of a series of cases. Serum concentrations of BDNF during the immediate puerperium was compared among women with crack dependence, recruited at two large hospital, vs healthy mothers, derived by mothers who accepted to donate the cord blood of their babies to Bank Umbilical Cord Blood and Placenta of our institution. The levels of BDNF were measured in peripheral blood.
Results: The sample was comprised by 29 women with crack dependence and 29 healthy mothers. In the crack group there were more single mothers (33.3% vs zero, p 0.001) and non-white ethnicity (76.5% vs 23.1%, p = 0.001). BDNF level at the delivery time was significantly higher among women who consumed crack during pregnancy (median = 44.86) in comparison to non-drug addicts (median 28.11. Mann-Whitney U = 285, Z= -2.17, p = 0.035).
Conclusions: To the best of our knowledge, this is the first study that documents the BDNF levels in women who were users of crack during pregnancy measured in peripheral blood after delivery. It seems that the process of adaptive increased of BDNF in order to seek a neuronal survival, caused by crack consumption, is kept under pregnancy conditions.
Financial Support: SENAD and CAPES, Brazil

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HIGH GENETIC RISK FOR METHAMPHETAMINE INTAKE IN MICE RELATES TO PERTURBATIONS IN NEUROTRANSMISSION IN MEDIAL PREFRONTAL CORTEX AND NUCLEUS ACCUMBENS.

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Aims: The recent creation of methamphetamine (MA) high and low drinking (MAHDR and MALDR) selected lines of mice that also exhibit high versus low sensitivity to MA rewardt enable the exploration of the neural underpinnings of genetic risk for MA addiction. Thus, this study aimed to relate genotypic differences in MA reward to extracellular levels of neurotransmitters within the medial prefrontal cortex (mPFC) and nucleus accumbens (NAC).
Methods: In vivo microdialysis was used to quantify basal levels of serotonin, dopamine and glutamate, as well as the capacity of a 2 mg/kg MA injection to elevate neurotransmitter levels, in female mice from the MAHDR and MALDR selected lines, as well as female mice from the F2 cross of the C57BL/6J and DBA2/J inbred strains (B6D2F2).
Results: Genotypic differences in basal extracellular neurotransmitters were observed for mPFC and NAC dopamine (MAHDR<MALDR=D2B6, for mPFC and NAC glutamate (MALDR <MAHDR=D2B6) and for NAC serotonin (MAHDR>MALDR=D2B6). Genotype differences were also observed regarding MA-stimulated neurotransmitter release for mPFC dopamine (MAHDR>MALDR=B6D2), mPFC serotonin (MAHDR<MALDR=B6D2) and NAC glutamate (MALDR<MAHDR=B6D2).
Conclusions: Together, these data indicate perturbations in both monoaminergic and glutamatergic systems within the corticoaccumbens pathway as genetic correlates of a high MA-consuming phenotype.
Financial Support: This work was supported, in part, by NIDA grant R01DA024038 to KKS, the Department of Veterans Affairs and NIDA grant P50 DA018165 to TJP.

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NEURAL TRACKING OF PREDICTION ERROR (PE) IS REDUCED IN SUBSTANCE-DEPENDENT INDIVIDUALS.

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Aims: Substance dependent individuals (SDI) make poor decisions on the Iowa Gambling Task (IGT), a task that simulates real-life decisions involving risk and uncertainty. Decision-making depends upon several factors, including how sensitive individuals are to feedback and how well they learn based on such feedback. A physiological signal, driven by striatal dopamine, that guides learning and decision-making based on feedback is prediction error (PE). Hypothesis: Compared to controls, SDI would show alterations in the neural tracking of PE during decision-making on a modified IGT (mIGT).
Methods: Thirty-two SDI and 30 controls played the mIGT during fMRI scanning. Behavior was analyzed using a cognitive model which identifies psychological processes underlying IGT performance (Stout et al., 2004). For each trial, the model computes a prediction error (PE), the difference between predicted and expected outcome. Tracking of PE was compared across group using a 2-sample t-test. Statistical threshold was set at voxel-level of $p < 0.005$, uncorrected, and $p < 0.01$ whole-brain cluster-corrected, corresponding to an extent threshold of 39 voxels based on 10,000 Monte Carlo simulations.
Results: Consistent with previous work on the IGT, the cognitive model parameters indicated that compared to controls, SDI made more erratic choices ($p=0.02$) and demonstrated a trend toward lower sensitivity to loss ($p=0.06$) on the mIGT. SDI did not track trial-to-trial PE learning signals as strongly as the Controls in the striatum, medial orbitofrontal cortex, and insula.
Conclusions: Better tracking of PE signals in controls compared to SDI suggests that a possible mechanism of poor decision-making in substance dependence may involve disruptions in PE learning processes. Group differences in striatal and OFC suggest that frontal-striatal pathways may represent targets for future therapies in drug addiction.
Financial Support: National Institute of Drug Abuse DA024104 and DA02774

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CJDATS2 LOCAL CHANGE TEAM INITIATIVES FOR IMPROVING ASSESSMENT FOR DRUG TREATMENT IN CORRECTIONAL SYSTEMS.

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Aims: CJDATS2 is a NIDA-funded national initiative to implement and evaluate organizational and process improvement strategies within correctional systems. Goals for this multisite project include identifying and addressing gaps in assessment, service planning, and service delivery for offenders as they transition from correctional custody to community treatment. Each research site includes representatives from a partnered prison system and a community treatment provider to form a local change team (LCT). In collaboration with an external facilitator, the LCT then identifies areas for improvement in the process of offender assessment, and develops a Process Improvement Plan (PIP) to address these needs. This paper provides a brief overview of the Assessment component of the CJDATS2 initiative, and describes the strategies selected by the LCTs to improve the assessment and case planning process.
Methods: CJDATS2 includes 9 research centers. Using the Organizational Process Improvement Intervention (OPII), each site formed an LCT and developed a Process Improvement Plan. The authors examine the goals and objectives of these plans to identify common themes and the range of interventions identified by the LCTs for improving the assessment process within correctional systems.
Results: Among the targeted areas in the Process Improvement Plans were strategies for improving the conveyance of assessment information from prison to community corrections systems, adopting new assessment instruments for substance abuse as well as other areas of offender functioning, and developing new methods for consolidating and integrating assessment information in case plans for improved continuity of care.
Conclusions: The OPII may prove useful in creating dialogue between agencies regarding high priority treatment needs in the substance abuse assessment process and in outlining the steps to address these needs.
Financial Support: This study was funded by the National Institute on Drug Abuse (NIDA).

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WITHDRAWN

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INTEGRATION OF SUBSTANCE USE DISORDER TREATMENT WITH PRIMARY CARE IN PREPARATION FOR HEALTH CARE REFORM.

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Aims: As a result of the Affordable Care Act, substance use disorder (SUD) services are expected to become more integrated with primary care. However, the data on the state of integration is currently limited. Our aims are to:
(1) Describe the state of SUD services and integration in federally qualified health centers (FQHCs)
(2) Examine barriers and facilitators of integration from the provider/other stakeholder perspectives
(3) Recommend changes in policy to support integration efforts
Methods: Mixed quantitative and qualitative research methods were used to investigate specific SUD-related practices and the integration with primary care. A web-based survey was conducted among FQHCS in 5 California counties. Descriptive data analyses were performed to characterize the nature of the services and models/levels of SUD service integration. Providers/other stakeholders from three FQHCs (n=18) were interviewed to gain a more in-depth understanding of integration efforts. Qualitative data were analyzed using Atlas.ti.
Results: Fourteen FQHCs completed the survey (78% response rate). Half of the FQHCs reported close collaboration between SUD and primary care, but the other half indicted only minimal or basic levels of integration. SUD services are generally not as well integrated with primary care as mental health services are, are rated as less effective, and are separated from primary care services physically and temporally; use of common evidence-based practices is moderate. Barriers to SUD integration include inadequate workforce training, billing restrictions/requirements, and limited specialty SUD services in the community for patient referrals. Facilitators of integration include easy access to behavioral health specialists, providers with the right "fit", and an organizational culture supportive of innovation. Policy recommendations will be presented.
Conclusions: Some integration of SUD services with primary care is occurring, but SUD practices vary widely, and there is more work to be done. Policy changes are needed to support and facilitate integration.
Financial Support: California Program on Access to Care #KKN06A

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ADOLESCENT AND EMERGING ADULT MARIJUANA TRIERS AND NON-USERS: THE DIFFERENCE IN POTENTIAL HIV RISK.

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Aims: The combination of substances and risky sexual behavior increases the likelihood of contracting HIV. Two behaviors that have been linked to one another include marijuana use and risky sex. Previous research has attempted to examine decision making as an underlying behavioral mechanism contributing to increased risk behavior during adolescence. The present study aimed to examine decision making differences in marijuana smoking status groups and subsequent HIV risk.
Methods: For the current study, we examined patterns of HIV risk in two different marijuana smoking status groups (Non-smokers and Triers) using Analysis of Variance (MANOVA). The study utilized a sample of adolescents and emerging adults (N=87, Non-Smokers = 52 and Triers = 35).
Results: The MANOVA revealed significant decision making differences between marijuana triers and non-users on both the Delay Discounting Questionnaire ($F(1) = 3.847$, $p = 0.053$) and the Sexual Discounting Task ($F(1) = 6.668$, $p = 0.011$)- where triers discounted delayed rewards more so than non-users. Next, differences between smoking status groups and HIV risk behaviors that would result from poor decision making were examined- Triers were found to be more significantly ($p < 0.05$) sexually risky than non-users: earlier age of onset for Kissing ($F(1) = 16.538$), French Kissing ($F(1) = 18.361$), Touch Breasts ($F(1) = 22.019$), Touch Penis ($F(1) = 24.16$), Touch Vagina ($F(1) = 29.760$), Oral Sex ($F(1) = 24.662$), Vaginal Sex ($F(1) = 27.131$), Oral Sex condom use frequency ($F(1) = 16.623$, Vaginal Sex condom use frequency ($F(1) = 10.275$, Anal Sex condom use frequency ($F(1) = 4.879$ as well as ever having unprotected Oral ($F(1) = 12.517$), Vaginal ($F(1) = 15.230$), and Anal ($F(1) = 4.230$) sex.
Conclusions: These findings indicate that marijuana smoking status may relay differences in HIV risk and that these differences are likely attributable to difference in decision making. Future research efforts should examine triers, an understudied group that is vulnerable for HIV risk.
Financial Support: The study was financially supported by Dr. Sherecce Fields, faculty start-up funds.

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RECOVERY-ORIENTED CARE IN AMERICAN-INDIAN COMMUNITIES: A CULTURALLY LEGITIMATE PRACTICE IN INDIAN COUNTRY.

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Aims: To determine how a ROSC can be culturally adapted to American Indian substance abuse recovery.
Methods: Substance use disorders are considered a chronic disease and clients in recovery need support from their entire community to be able to maintain sobriety. The shift in service delivery from acute to long term care is often referred to as Recovery Oriented Systems of Care (ROSC). Prairielands ATTC in partnership with the GPTCHB, Northern Plains Behavioral Health Programs, has held talking circles with a number of tribal behavioral health professionals both in the Northern Plains and Great Lakes regions to explore how this national movement can best be adapted to Native American recovery. Four talking circles (focus groups) were completed in four different tribal communities in the Upper Mid-West, and between 8 to 10 tribal providers participated in each of the talking circles completed.
Results: The majority of the participants found that the basic principals and philosophy of ROSC follow many of the teachings of the American Indian culture: supporting the community members in their recovery. However, the resources to implement the changes are lacking, such as the use of Drug courts, collaboration with the treatment community with the Bureau of Indian affairs. Suggestions were also made that urban indian communities may be better able to follow the ROSC principals.
Conclusions: The ROSC model contributes to the intrinsic values of Native American culture and compliments the historic movement towards the red road to recovery.
Financial Support: This study was completed by Prairielands ATTC under a cooperative agreement from SAMHSA.

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SUBSTANCE USE DISORDERS AND POVERTY AS PROSPECTIVE PREDICTORS OF FIRST-TIME SUICIDE ATTEMPT IN THE UNITED STATES.

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Aims: Substance use disorders (SUD) and poverty are strongly associated with suicide attempt in the United States. However, their joint influence on first-time adult suicide attempt has not been prospectively examined in national data. This study examined whether SUD and poverty predicted first-time adult suicide attempt over three years.
Methods: Participants were interviewed in Waves 1 (2001-2002) and 2 (2004-2005) of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC). Wave 1 DSM-IV SUD were measured by the AUDADIS. Household poverty was calculated using 2001 federal poverty guidelines, adjusted for household size, income, and state. Those with no history of suicide attempt at W1 (N=33,750) were analyzed. Logistic regression models estimated main and interaction effects of SUD and poverty on first-time suicide attempt, adjusted for demographic, psychiatric, and ecological variables.
Results: Of the sample, 0.4% (N=145) were first-time suicide attempters by W2. Experiencing poverty (OR=2.27, CI=1.51-3.42) and both alcohol and drug use disorders (OR=7.43, CI=2.71-20.37) independently increased prospective odds of W2 first-time suicide attempt. The effect of drug use disorders was significantly moderated by poverty, differentially increasing risk for first-time suicide attempt by 49.7% ($p<.001$).
Conclusions: This is the first study to prospectively examine the joint influences of substance use disorders and household poverty on subsequent adult first-time suicide attempt in national data. Both SUD and poverty increased the risk of first-time suicide attempt. Further, the combination of drug use disorders and poverty created significantly greater risk for the first-time incidence of suicide attempt than the sum of risks associated with these factors considered separately. Substance abuse treatment should address how current financial status may increase future risk of suicide attempt. This study reinforces the importance of both SUD and poverty in the risk for first-time suicide attempt and can serve as a benchmark for future studies.
Financial Support: K23DA032323, U01AA018111, K05AA014223.

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VIRTUAL REALITY-INDUCED CRAVING FOR CIGARETTES AMONG ABSTINENT SMOKERS.

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Aims: To evaluate cue induced craving among nicotine-dependent cigarette smokers exposed to smoking-related active and neutral virtual-reality cues.
Methods: Cigarette smokers were evaluated in a sated condition (Day 1) and during nicotine withdrawal (24 h abstinent: Day 2). Self-report measures on nicotine withdrawal and craving (Visual Analog Scales: VAS, Wisconsin Symptom Withdrawal Scale: WSWS, and Questionnaire of Smoking Urges: QSU) and physiological (blood pressure/heart rate) responses were determined in response to active and neutral smoking cues presented in a virtual reality environment.
Results: To date, 11 cigarette smokers have been enrolled (target N=60). The participants are 36.1±3.7 years of age (mean±S.E.M.), self-report smoking 13.8±2.2 cigarettes per day (CPD) and have average Fagestrom Test for Nicotine Dependence scores of 3.5±0.7. Participants differed significantly from Day 1 (17.1±3.1) vs. Day 2 (5.1±1.4) for breath carbon monoxide ($p<0.0005$) indicating that they successfully abstained overnight. In comparison to neutral cues, exposure to active virtual reality cues (smoking paraphernalia, party scenes) led to significantly higher ratings of several adjectives, including "Craving for Cigarettes" ($p=0.006$) and "Thinking About Cigarettes" ($p=0.0009$). In addition, there were significant positive correlations between Craving for Cigarettes and QSU scores ($r=0.85$, $p<0.001$) and WSWS scores ($r=0.60$, $p=0.053$).
Conclusions: The current data illustrate our ability to recruit cigarette smokers and evaluate their subjective and physiological responses. More importantly, the results reveal that virtual reality cues engender robust craving responses for nicotine in a laboratory setting. Additional data for this project will include evaluations of neural responses during a passive learning task using fMRI, and determination of the extent to which a specific SNP in the nicotinic receptor α5 gene mediates the observed behavioral effects.
Financial Support: Funding provided by the Helis Medical Research Foundations. This work was conducted at the MEDVAMC, Houston, TX

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A PROSPECTIVE STUDY OF ALEXITHYMIA AND CRAVING AMONG ALCOHOL-DEPENDENT TREATMENT SEEKERS.

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Aims: Up to 50% of alcohol-dependent patients in treatment suffer from alexithymia, a personality trait associated with mood regulation difficulties. Other factors such as obsessive thoughts and compulsive drinking behaviors conceptualized as craving are also considered key factors associated with the loss of control over drinking. However, no longitudinal study has investigated the relationship of alexithymia and craving among patients with alcohol problems. The aim of the present study was to explore this relationship and to test the relative contribution of alexithymia in predicting craving after controlling for comorbid anxiety and depression.
Methods: 93 consecutive patients (72% male), 18-66 years of age, undertaking Cognitive-Behavioral Therapy for alcohol dependence were assessed before the commencement (baseline) and at the end (12 weeks-follow-up) of a treatment program. Participants were detoxified prior to assessment and completed the Toronto Alexithymia Scale (TAS-20), the Anxiety and Depression subscales of the General Health Questionnaire (GHQ) and the Obsessive Compulsive Drinking Scale (OCDS).
Results: At baseline TAS-20 total score, Difficulties Identifying Feelings (DIF) and Difficulties Describing Feelings (DDF) were significantly positively associated with GHQ anxiety and depression scores, OCDS total score, obsessive thoughts about alcohol scores as well as compulsive drinking urges and behavior scores. Multiple regression analyses controlling for baseline age, gender, anxiety and depression identified that alexithymia were associated with higher OCDS total score and obsessive thoughts about alcohol at 12 weeks follow-up.
Conclusions: These findings highlight the importance of alexithymia as a prospective predictor of alcohol craving among alcohol-dependent treatment seekers.
Financial Support: No financial support.

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A BRIEF MEASURE ASSESSING SEXUAL RISK BEHAVIOR IN WOMEN IN SUBSTANCE ABUSE TREATMENT.

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Aims: Sexual risk behavior is common among substance abusers. To effectively target sexual risk behaviors for intervention in treatment programs, it is important to have a rapid and accurate measure of sexual risk. This study compares two dichotomous ratings of unprotected sex (Y/N) among women in outpatient substance abuse treatment who participated in a NIDA Clinical Trials Network HIV sexual risk reduction intervention: 1) any unprotected sex during vaginal or anal sex occasions in the past 3 months versus 2) unprotected sex at last sexual occasion.
Methods: 363 sexually active women with a main or non-main male partner(s) from 12 methadone maintenance or psychosocial outpatient treatment programs were included. Unprotected sex in the last 3 months (dichotomized as yes/no) and unprotected sex at last occasion (yes/no), combined across 3 time points (baseline, 3-month and 6-month follow up), were compared for congruence.
Results: Considering sexual occasions with main male partners (n=787 occasions), 87.8% of the sample reported unprotected sex in the past 3 months compared to 93.1% reporting unprotected sex at last occasion. Only 1.3% (n=10) were incongruent (reported unprotected sex at last sexual occasion but consistent protection during the last 3 months). Considering sexual occasions with non-main partners (n = 182), 68.1% of the sample reported unprotected sex at last occasion, compared to 61.5% reporting unprotected sex in the past 3 months. 8 results (6.5%) were incongruent.
Conclusions: Dichotomous ratings of unprotected sex at last sexual occasion and unprotected sex in the past 3 months similarly categorized the vast majority of women in substance abuse treatment programs. In busy substance abuse treatment programs, a single question about last sexual occasion could efficiently identify the presence of sexual risk behavior, and provide a basis for selected sexual risk reduction intervention.
Financial Support: This study was supported by National Institute on Drug Abuse (NIDA) Clinical Trials Network grants: U10 DA13035 (Edward Nunes, PI)

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EFFECTS OF WALKING ON CIGARETTE CRAVING, NICOTINE WITHDRAWAL SYMPTOMS AND AFFECT IN SMOKERS WITH SCHIZOPHRENIA.

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Aims: The mortality rate of people with schizophrenia is two- to three-times that of the general population, primarily because of elevated rates of cigarette smoking, physical inactivity, obesity, elevated blood cholesterol, hypertension and diabetes mellitus. Numerous studies have found that aerobic exercise acutely reduces cigarette craving among smokers without psychiatric illness. The aim of the current exploratory/developmental project is to determine whether a brief session of aerobic exercise also reduces cigarette craving and smoking behavior among people with schizophrenia.
Methods: Participants (current n = 10) undergo an initial session in which they complete baseline individual difference measures and habituate to walking on a treadmill, followed by 4 study sessions consisting of a cue exposure period (smoking cues or neutral control cues), followed by an activity period (1 mile treadmill walk or inactive control). Measures include cigarette craving, nicotine withdrawal symptoms (MNWS; Hughes & Hatsukami, 1986) and positive and negative affect (PANAS; Watson et al., 1988).
Results: Results among participants who have completed the study to date (70% male; age 40.5 ± 12.6 yrs, smoke 21.3 ± 12.3 cigs per day, body mass index [BMI] = 30.3 ± 6.0) indicate that, relative to the inactive control condition, the 1-mile walk tends to reduce craving, with a large effect size (pre-post change scores: Walking = -1.17 ± 0.57; Control = -0.25 ± 0.28; $p < .08$; partial eta2 = 0.49), significantly reduces nicotine withdrawal symptoms (pre-post change scores: Walking = -.38 ± 0.1; Control = -.03 ± .09; $p < .05$; partial eta2 = 0.69) and tends to increase positive affect, with a large effect size (pre-post change scores: Walking = +4.75 ± 0.94; Control = +0.42 ± 1.3; $p = .09$; partial eta2 = 0.47).
Conclusions: These findings suggest that walking could be an effective "rescue strategy" for reducing craving and other mood triggers for smoking among people with schizophrenia, and support the idea of including walking in smoking cessation interventions for people with serious mental illness.
Financial Support: Supported by R21DA031283.

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BUPRENORPHINE VS. MORPHINE WITHDRAWAL: A CONTROLLED COMPARISON.

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Aims: Preliminary evidence suggests there is relatively little spontaneous withdrawal following cessation of chronically administered buprenorphine (BUP) and that withdrawal symptoms are delayed compared to other opioids. However, few controlled human studies have systematically studied BUP withdrawal.
Methods: Healthy, out-of-treatment opioid dependent volunteers (N=7) were enrolled in a 59-day residential study of spontaneous opioid withdrawal from BUP versus morphine (MOR). Volunteers were stabilized either on double-blind intramuscular (IM) BUP (32 mg/day) or MOR (120 mg/day) administered in 4 divided doses for 9 days. They then underwent an 18-day period of spontaneous withdrawal, receiving 4 double-blind IM placebo injections daily. Stabilization and spontaneous withdrawal were then repeated for the 2nd opioid. Standard withdrawal measures were collected daily. Repeated measures two-factor (withdrawal condition, time) ANOVA was performed to assess differences.
Results: Volunteers were male, 86% African American, had a mean age of 49 years, and had used heroin for a mean of 9.6 years. There were significant ($p<.05$) differences between the 2 withdrawal conditions on mean peak ratings of: subjective opiate withdrawal scale (SOWS); clinical opiate withdrawal scale (COWS); all subscales of the Profile of Mood States (POMS); sick and pain (0-100) visual analog scales (VAS); systolic and diastolic blood pressure; heart rate; respirations; and pupil dilation. There were also significant ($p<.0001$) condition-by-time differences on SOWS, COWS, and pupil dilation. Mean peak ratings on SOWS (28.4) and COWS (12.6) occurred on day 2 of MOR withdrawal and were significantly different ($p<.05$) from day 2 of BUP withdrawal (4.1 and 1.3, respectively). Subjective complaints of MOR withdrawal resolved on average by day 7. There was little evidence of BUP withdrawal on any of the measures across the 18 day period.
Conclusions: Spontaneous BUP withdrawal is subjectively and objectively milder as compared to MOR for at least 18 days after drug cessation.
Financial Support: DA08045, DA023186, DA029609-01A1.

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THE IMPACT OF PERSONALIZED FEEDBACK ON MARIJUANA USE: EXAMINING A BRIEF INTERVENTION DELIVERED VIA THE INTERNET.

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Aims: Marijuana remains the most commonly used illicit drug in the United States, and many people who experience problems related to their marijuana use do not seek treatment. Web-based interventions for problematic marijuana use represent a potentially cost-effective way to reach those who are ambivalent about changing their marijuana use or are concerned about seeking in-person counseling. The goal of this study was to evaluate the effectiveness of a brief web-based feedback intervention for marijuana users with problematic marijuana use.
Methods: Adult college students who reported at least some problems related to marijuana use were randomized to either a personalized feedback report condition or an education-only control group. Reports were delivered to participants after completion of a baseline assessment, and participants were reassessed at 1- and 3-months post-baseline. Primary outcome variables were problems related to marijuana use and frequency of use. Analyses examined change over time by condition as well as possible moderating variables of Stage of Change and family history of problematic substance use.
Results: To date, the sample includes 82 participants. Both marijuana-related problems, $F(1, 32) = 7.06$, $p = .01$, and frequency of marijuana use, $F(1, 33) = 10.30$, $p = .003$, decreased between baseline and the one-month follow-up, but there were no significant interactions by condition. These reductions were not sustained at three-months. However, effect sizes across several outcome variables, including frequency of use and symptoms of dependence, were in the medium range.
Conclusions: Analyses did not support the hypothesis that personalized feedback would lead to greater reductions in outcomes compared to a control group, but several trends in the data are promising. Data collection is ongoing and results may improve with increased sample size. This research represents an important step in developing empirically-supported online interventions for marijuana users, given the popularity of the internet as a source of health information.
Financial Support: None

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INTEGRATING SUBSTANCE USE DISORDER SERVICES INTO PRIMARY CARE SETTINGS: CURRENT STATUS IN CALIFORNIA.

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Aims: Due to health care reform, integration of substance use disorder (SUD) services into primary care settings has taken on increased urgency. Our aim is to quantify current integration efforts in California using a variety of methods, including surveys, site visits, and interviews.
Methods: UCLA conducted the following to determine the status of integration in California:
1) An online survey of county Alcohol and Drug administrators on integration efforts in their counties.
2) The Dual Diagnosis Capability in Health Care Settings (DDCHCS) tool to measure integration processes in primary care settings.
3) Staff interviews and perception surveys to measure staff views.
Results: We found that:
1) Integration is currently underway.
2) Integration is increasing in organizations that are working on it.
3) There were differences between medical and behavioral health staff perceptions of SUD services.
Conclusions: Integration is a good thing and is starting to work, but barriers remain and there is a lot of work to do around the state. Challenges ahead remain in utilizing current data systems for integration measurement as well as measuring its impact on health care costs. With much training and technical assistance, preparing for health care reform is necessary.
Financial Support: California Department of Alcohol and Drug Programs; Kern County

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CHRONIC METHYLPHENIDATE ELICITS LONG-TERM EFFECTS IN ADOLESCENT FEMALE WKY RATS.

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Aims: The biological rhythm in animals is governed by the clock genes. Changes in circadian rhythm are results of molecular changes in the circadian gene clock. Our hypothesis is that changes in circadian activity by a drug indicate long term effects. This study aims to investigate the effects of methylphenidate (MPD) on adolescent female WKY rats circadian activity pattern.
Methods: Animals were divided into 4 groups. On experimental day 1 (ED1), all groups received saline injection. On ED2 to 7, each of the 4 groups received saline, 0.6, 2.5, or 10.0mg/kg of MPD. ED8 to 10 were washout days. On ED11, they were again given the same treatment as ED2 to 7. Locomotor activity was recorded post injection non-stop for 11 consecutive days using open-field assay.
Results: Hourly histograms and SCCA calculating the acrophase (Φ), amplitude (A), and mesor (M) were used to assess the 24-hour circadian activity pattern. Comparing ED2 to ED1, all groups showed increased locomotor activity but were insignificant. At ED7 vs. ED2, the 2.5 and 10mg/kg groups showed significant changes in the locomotor activity ($p=0.009$ and $p=0.001$, respectively). At ED8 vs. ED1, the 10mg/kg group showed significance ($p<0.05$) decrease in mesor and amplitude. At ED11 vs. ED2, the 0.6mg/kg group showed a decreased mesor ($p=0.039$); the 2.5mg/kg group showed an increased mesor ($p=0.033$); the 10mg/kg group showed decreased mesor and increased amplitude. ($p=0.000$).
Conclusions: There was a rhythmic increase in locomotor activity during the dark period and a decrease in activity in the light period. 0.6 mg/kg failed to elicit change in locomotor activity pattern in ED2 and 7 but was able to alter the activity pattern at ED11. The 2.5 and 10.0 mg/kg MPD doses elicit an increased average locomotor activity in all days and modulate the circadian locomotor activity pattern in ED 7, 8, and 11, suggesting that all doses have long term effect on animal behavior. These long-term changes suggest that permanent changes at the molecular level occurred, expressed by tolerance, sensitization and even in the circadian gene clock that result in alteration in the circadian rhythm activity pattern.
Financial Support: NIH RO1 DA027222

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PTSD AND SUBSTANCE ABUSE COMORBIDITY FROM A BEHAVIORAL ECONOMIC PERSPECTIVE.

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Aims: Posttraumatic Stress Disorder (PTSD) and substance abuse are common among combat veterans. Behavioral economic research suggests that substance use is more likely when the relative reinforcing value of a substance is high. For veterans with PTSD, it is important to understand the full context in which substance abuse occurs (including both substance-related and substance-free activities). This study examined the relationship between PTSD symptoms and both substance-related and substance-free reinforcement over time.
Methods: Participants were 68 veterans who were recruited from a VAMC primary care clinic, screened positive for alcohol misuse (AUDIT) and then received a brief alcohol intervention. 60% of the sample met criteria for PTSD. They completed the Activity Level Questionnaire assessing frequency and enjoyment associated with a range of activities over the past 30 days. Data were collected at baseline and 6 month follow-ups.
Results: Pearson correlations assessed relationships between PTSD symptoms and substance-related and substance-free reinforcement. At baseline, reexperiencing, numbing, and hyperarousal symptoms were strongly inversely correlated with substance-free reinforcement ($r = -.36, -.50, -.40$, respectively). Only hyperarousal symptoms were positively associated with substance-related reinforcement ($r = .32$). Baseline numbing symptoms remained a significant predictor of substance-free reinforcement at the 6-month follow up ($r = -.50$).
Conclusions: While substance abuse among individuals with PTSD is often considered to serve a self-medication function, these data suggest that a dearth of positive reinforcement from substance-free activities, a consequence of PTSD-related anhedonia, may also drive this relationship.
Financial Support: National Institute on Alcohol Abuse and Alcoholism (NIAAA); Veterans Affairs Medical Center, Memphis

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THE SUBSTANCE AND ILLICIT DRUG ABUSER MIGRATION FROM URBAN TO RURAL AREA IN TAIWAN POPULATION BETWEEN 2005 AND 2009.

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Aims: The earlier study in Taiwan presented the higher substance abuse in urban area before 2005. The purpose of our study was to examine the prevalence of these risky behaviors among Taiwan adults in different years.
Methods: A national population-based cross-sectional survey. Secondary Data analyzed from the 2005 and 2009 National Health Interview Survey in Taiwan. We used the data containing personal socioeconomic status and addictive materials information including history of smoking, drinking, chewing betel nuts and material use behaviors for measuring their substance usage pattern. The GIS system presented the substance and drug abuse risk map.
Results: The results showed the increasing prevalence in alcohol use from 2005 to 2009 (50.4% to 60.4%). In the other hand, the cigarette, sedatives usage was decreasing significantly in the year 2009 (38.6% to 35.5% for cigarette; 2.9% to 1.1% for sedatives). In multivariate analysis for estimating the risk of substance usage by different county/city in Taiwan, the higher risks of cigarette, betel nuts and illicit drug use were changed from north urban cities/counties to rural area in south east of Taiwan. The higher risks were shown in larger cities and south east rural area in 2009. Comparing with the capital city, the odds ratio of illicit drug use were significantly higher both in a satellite city of capital and a rural south east county, which are 2.47 (1.29, 4.75; 95%CI) and 2.52 (1.21, 5.23; 95%CI) in 2009.
Conclusions: There were two substance usage related policies in Taiwan between 2005 and 2009. First, Taiwan had Tobacco Health and Welfare Taxes levied in both 2002 and 2006 which might affect the cigarette usage in 2009. Second, the harm reduction started in 2004-2005 might affect illicit drug prevalence changing through time. The further reason of drug users migration must be follow up for control the substance abuse.
Financial Support: A grant from the Taiwan Food and Drug Administration (DOH101-TFDA-N-004)

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DEPRESSSION, PAIN CATASTROPHIZING AND PAIN TOLERANCE IN OPIOID-DEPENDENT PATIENTS.

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Aims: Patients with opioid dependence on opioid agonist treatment (OAT) are at risk for chronic pain and hyperalgesia/pain intolerance. This study examined whether depression and pain catastrophizing were associated with either pain tolerance or self-reported pain in sample of treated opioid dependent patients.
Methods: This cross-sectional study included opioid dependent adults on OAT (methadone or buprenorphine). Dependent variables were: 1) pain tolerance (cold-pressor test) and 2) self-reported pain as it interfered with daily living (subscale from the Brief Pain Inventory). Independent variables were pain catastrophizing (Pain Catastrophizing Scale) and depressive symptoms (PHQ9). Additional covariates were age, gender, race, duration and type of OAT. Pearson correlations and t-tests results are reported; multivariate regression analyses are planned.
Results: Participants (n=40) had a mean age 44(SD±9) years, were 45% female, 30% non-white. The median duration on OAT was 2 years; 22% were on methadone. The majority (83%) had chronic pain (>6 months). Pain tolerance was not correlated with depressive symptoms (r=-0.11, p=0.47) or pain catastrophizing (r=0.03, p=0.84). Pain interference was significantly correlated with depressive symptoms (r=0.37, p=0.02) and pain catastrophizing (r=0.41, p=0.009). Likewise, there was no significant difference in mean pain tolerance among participants with more depressive symptoms (p=0.14) or pain catastrophizing (p=0.61); however, participants with more depressive symptoms and pain catastrophizing had significantly higher levels of self reported pain that interfered with daily living (p=0.02 and p=0.01, respectively).
Conclusions: Results suggest that pain catastrophizing and depression are associated with self-reported pain, but not experimental pain tolerance in a sample of opioid dependent patients on OAT.
Financial Support: This study is supported by NIH/NIDA grant K23DA027367

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A RANDOMIZED TRIAL COMPARING REINFORCEMENT-BASED TREATMENT WITH AND WITHOUT PERSONALIZED PATIENT FEEDBACK.

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Aims: The primary aim of the study is to examine the contribution of feedback (an adaptation of motivational interviewing) on the short term treatment outcomes for patients receiving reinforcement-based treatment (RBT).
Methods: A total of 23 patients participating in outpatient treatment were consented and randomly assigned to receive RBT as usual, which includes personalized feedback (RBT: n=12) or to RBT without feedback (RBT-FB: n=11). Primary outcome variables included drug positive urinalysis results at thirty days post treatment enrollment (yes/no drug positive), retention in treatment at thirty days (yes/no whether retained in treatment for the thirty days), and days of treatment attendance (number of days attended during first 30 days).
Results: Participants in the two conditions were similar on demographic variables: on average they were 37.7 [11.06] years of age, had earned an average of 12.0 [2.21] years of education, were predominately single (87%), female (65%), and the majority were African American (57%). They were also similar on pre-treatment drug use variables, with an average of 6.22 [10.15] days of opioid use, 3.96 [8.91] days of cocaine use, and 14.04 [11.32] days of alcohol use. There were no significant differences between the two conditions on the one month outcome measures of drug positive urine results at one month (RBT=36% versus RBT-FB=63%, p=.370), or days of treatment attendance (RBT=21.75 [2.83] days versus RBT-FB=19.45 [5.94] days, F=1.440, p=.243).
Conclusions: Preliminary results show no significant differences between participants receiving RBT versus those receiving RBT-FB. However, the current sample size of 23 may be insufficient to detect differences on key outcome variables. The study is ongoing and it is estimated that we will reach a sample size of N=47 for analysis and presentation at the June CPDD meeting.
Financial Support: Research was conducted as part of standard care practice and no participant compensation was provided.

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CHARACTERISTICS OF PERINATAL WOMEN SEEKING TREATMENT FOR MARIJUANA ABUSE IN A COMMUNITY-BASED CLINIC.

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Aims: In the US, marijuana continues to be the most frequently used illicit drug among women of childbearing age, including pregnant and postpartum women. While the consequences on the fetus remain equivocal, marijuana use during pregnancy has been implicated with neonatal morbidity. Associated risks extend into the postpartum period, including child abuse and neglect, and the removal of children from their homes. Given the critical window for treatment during the perinatal period, more information is needed about the characteristics of women who abuse marijuana and their unique needs with the goal of improving clinical services and outcomes for both women and their infants. Aims: To identify a profile of perinatal women seeking treatment for primarily marijuana abuse, and report birth outcomes in subset of women with marijuana abuse who were pregnant.
Methods: This retrospective clinical chart review study examined 67 adult perinatal women patients (44% Caucasian) who attended an inner-city, hospital-affiliated outpatient program specializing in substance abuse treatment for pregnant and postpartum women. The average age was 24 years (SD = 4.1), 92% were without a partner, 46% of the women were high school graduates or received a GED, 96% reported a history of a psychiatric disorder, and 76% were currently unemployed or disabled. Women in the program were either pregnant (46%) or postpartum (54%).
Results: Of all pregnant women, 26% reported positive urine screens during the first trimester, 41% during the second trimester, and 27% during the third trimester. While the subset of pregnant women was small, exploratory results suggest that infants whose mothers continued to use marijuana during their pregnancies were born at a lower gestational age than mothers who abstained; $t(29) = 2.04$, $p < 0.05$.
Conclusions: Identifying potential barriers to treatment could help improve retention in community-based treatment programs during pregnancy and postpartum, a critical period to reduce marijuana use.
Financial Support: T32 AA007459

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CORRELATES OF DRUG USE SEVERITY AND HIV RISK BEHAVIORS IN COCAINE- AND OPIATE-DEPENDENT PATIENTS.

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Aims: Demographic features and psychological symptoms may predict drug use severity, and HIV risk behaviors in drug users seeking treatment. Understanding these relationships may help customize services to individual patients needs. This analysis aimed to characterize demographic and psychological symptoms associated with drug use severity, cravings, and HIV risk behaviors in a population dually dependent on cocaine and opioid.
Methods: The analysis used baseline demographic, psychological and drug use severity assessment from cocaine and opioid dependent participants admitted into methadone maintenance (N=77). The following instruments were collected: Beck Depression Inventory [BDI], State Trait Anxiety Inventory [STAI], Traumatic Life Event Questionnaire [TLEQ], PTSD Symptom Scale [PSS], pain [VAS], Barrett Impulsiveness Scale [BIS], HIV Behavioral Risk Assessment Battery [BRAB], Self-reported IV and non-IV drug use, Cocaine Selective Severity Assessment [CSSA], Addiction Severity Index [ASI], and Questionnaire of Smoking Urges [QSU]. Methadone dose during treatment week 5 was recorded. A correlational analysis (Spearman Rho) was conducted between these variables.
Results: Scores of psychological symptoms were frequently correlated with one another and tended to cluster in expected domains: depression, anxiety, pain, TLEQ, and PSS. These scores were also associated with impulsivity and cocaine cravings. In addition BDI scores correlated with IV drug use and smoking urges; STAI scores correlated with smoking urges but negatively with IV drug use. Pain correlated with drug use duration. Younger age and non-IV drug use correlated with more sexual risk behaviors. More severe drug use and younger age at intake were associated with higher methadone dose.
Conclusions: While conclusions based on correlational analyses are limited, the results suggest that psychological distress is associated with impulsivity, craving, drug use severity, and HIV risk behaviors.
Financial Support: NIDA: DA021808, DA023186, T32DA07209

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CORRELATES OF IMPAIRED COGNITIVE PERFORMANCE IN COCAINE- AND OPIOID-DEPENDENT PATIENTS.

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Aims: There is evidence for cognitive impairment in individuals with substance use disorders. The purpose of this analysis was to identify specific demographic and clinical characteristics associated with poorer cognitive performance in individuals dually dependent on cocaine and opioids who were stabilized on methadone for five weeks.
Methods: A correlational analysis (Spearman's rho) was conducted between outcome measures from a cognitive assessment battery and demographic and clinical variables for 77 participants.
Results: The following variables were associated significantly ($p < 0.05$) with poorer cognitive performance: higher age (worse psychomotor coordination, focused and divided attention, executive function, working memory, episodic memory), lower education (worse executive function), lower IQ as measured by Shipley's Institute of Living Scale (worse focused attention, executive function, working memory, episodic memory), greater lifetime and 30-day poly-drug use as assessed by the Addiction Severity Index (worse executive function), higher cocaine use severity ratings (worse focused and divided attention), more smoking urges as assessed by the Questionnaire on Smoking Urges (worse working memory, episodic memory), greater anxiety as measured by the State Trait Anxiety Inventory (worse working memory, episodic memory), greater PTSD Symptom Scale score (worse focused and divided attention, episodic memory), higher pain ratings on a visual analog scale (worse working memory, episodic memory), and greater impulsivity on the Barrett Impulsiveness Scale (worse focused and divided attention, working memory, episodic memory).
Conclusions: While conclusions based on correlational analyses are limited, this information regarding the correlates of cognitive impairment may be useful in tailoring substance abuse treatment to specific cognitive abilities and in targeting cognitive remediation interventions to the most impaired individuals.
Financial Support: DA021808, DA023186, DA07209

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SUBSTANCES VIEWED THROUGH THE LENS OF TRAUMA: SUBSTANCE EXPECTANCIES IN WOMEN WITH PTSD/SUD.

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Aims: One of the most prominent psychiatric disorders among those with substance use disorders(SUD) is posttraumatic stress disorder(PTSD).This study examined expectancies in women with current PTSD/SUD.Expectancies refer to benefits expected from using a substance,e.g, "I use to relieve flashbacks of PTSD."Only 1 other assessment scale has been developed for expectancies in PTSD/SUD patients, a 27-item measure for alcohol expectancies in male veterans. In contrast,we used a 12-item scale to examine expectancies of any/all substances in women with PTSD/SUD.Aims:examine expectancies in women with current PTSD/SUD; examine the relationship between expectancies and general psychiatric/PTSD symptoms; evaluate internal consistency of the PTSD/SUD Expectancy Scale(PSES).
Methods: Our study sample included 52 women outpatients with current PTSD/SUD as part of a NIDA funded grant.We conducted a posthoc analysis on data collected at one timepoint, using Pearson correlations to assess how general psychiatric/ PTSD symptoms (measured by 10 standardized instruments) related to expectancies. Cronbach's Alpha was computed to test internal consistency of the PSES.
Results: Women with current PTSD/SUD reported overall moderate levels of expectancies to resolve PTSD symptoms. Expectancies were significantly associated with dissociation, suicidality, and depression. The PSES showed excellent internal consistency(α =.82).
Conclusions: Women with PTSD/SUD evidenced clear awareness of using substances to resolve PTSD symptoms, which has important implications for clinical care.Second, an association between substance expectancies and specific PTSD-related psychopathology (dissociation, suicidality, depression) indicates a need to attend to these areas. Third, the PSES shows strong initial psychometric properties, showing potential utility as a brief, clinically relevant instrument for implementation in a wide variety of medical/specialty settings. Future research should further explore gender in substance expectancies given known gender differences in PTSD/SUD etiology/clinical presentation(e.g,women more likely to suffer sexual violence).
Financial Support: none

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ORAL D-AMPHETAMINE INCREASES SENSITIVITY TO NEGATIVE CONSEQUENCES ON AN ASSOCIATIVE LEARNING TASK IN COCAINE USERS.

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Aims: The purpose of this study was to examine the acute effects of d-amphetamine (AMPH) on sensitivity to positive and negative consequences in cocaine users.
Methods: Thirteen intranasal cocaine users (12 male, 1 female), reporting 3.7 days (SD=1.2) of cocaine use ($228.9, SD=115.4) per week, participated in this 3-session outpatient study to date. Participants completed a computerized stimulus classification task at 180 min following administration of oral AMPH (0, 10, 20 mg); dose order was randomized and double-blind. On some task trials, correct responses were followed by a gain of 25 points (+$0.10) but incorrect responses were not followed by any feedback (positive consequence trials). For other task trials, incorrect responses were followed by a loss of 25 points (-$0.10), but correct responses were not followed by any feedback (negative consequence trials). The primary outcome measure was % optimal responses made on positive and negative consequence trials.
Results: For the positive consequences condition, optimal responding increased as a function of trial block ($p<0.05$), but AMPH had no effect on performance relative to placebo ($p>0.05$). Under the negative consequences condition, optimal responding did not increase as a function of trial block ($p>0.05$), but the 10 mg dose of AMPH increased overall optimal responding by about 8% relative to placebo ($p<0.01$).
Conclusions: Associative learning increased over time only when the response consequences were positive, suggesting a biased sensitivity to reward (relative to loss) in these intranasal cocaine users. The 10 mg AMPH dose increased learning only when the consequences were negative, suggesting that a moderate dose of AMPH elevated sensitivity to loss in these cocaine users. Since elevated loss sensitivity in cocaine abusers has been associated with less frequent cocaine use, these data may point towards a therapeutic value of moderate doses of AMPH for cocaine dependence.
Financial Support: DA022282 (SCR)

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PRECOCIOUS TRANSITIONS AND INJECTION DRUG USE: A LONGITUDINAL STUDY OF MEXICAN-AMERICAN MALES.

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Aims: Injection drug use is highly associated with the spread of infectious diseases such as HIV. This study examines the relationship between experience of multiple "precocious transitions" in late adolescence and injection heroin use in adulthood among Mexican American men who are former gang members. Precocious transitions are premature transitions to adult roles and statuses such as dropping out of high school and early parenthood.
Methods: A random sample of 160 gang-affiliated Mexican American males was initially recruited for a study between 1996 and 1997 from 26 street gangs in San Antonio, Texas. Adolescents completed structured questionnaires and ethnographic interviews. A follow up study was conducted between 2009 and 2012 and 120 men from the original sample were re-interviewed. Retrospective data were collected on drug use patterns over a 10-year time period. A precocious transition index was created based on 5 binary outcomes: cohabitation, unemployment, school dropout, teenage parenting, and early nest-leaving. A one-way ANOVA was run to determine whether men with multiple precocious transitions reported more months of injection heroin use over time.
Results: Men who experienced multiple precocious transitions commonly reported cohabitation, dropping out of school, and unemployment. The mean number of months of injection drug use over 10 years was 12.6 years (s.d.=28.3). Men who experienced multiple precocious transitions engaged in significantly more injection drug use over time than did men with no or 1 precocious transition ($F=4.6$, $p=.035$). Men with multiple precocious transitions injected heroin for a mean of 16.6 months compared with a mean of 5 months for men with no or 1 precocious transition.
Conclusions: The experience of multiple precocious transitions places Mexican American adolescents involved with street gangs at risk for injection heroin use and infectious diseases. Subsequent analyses will determine the influence of multiple precocious transitions on specific drug use trajectories using the longitudinal retrospective data.
Financial Support: Funded by NIDA (Grant # 7R01DA023857)

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GENETICS-DRIVEN ANIMAL MODELS OF ADDICTION THROUGH NEXT-GENERATION SEQUENCING.

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Aims: This study aims to identify genetic variation in non-human primates that affects response to drugs, including drugs of abuse and their pharmaceutical therapeutics. This will increase our understandings of the genetic underpinnings of addiction and improve established non-human primate models for drug addiction research. This work refines the model, reduces unnecessary animal usage, and increases the translational validity of future studies.
Methods: Using array-based capture and next generation sequencing technologies, all non-olfactory G-protein coupled receptors were resequenced from genomic DNA in 40 Indian-origin rhesus, 24 Chinese-origin rhesus, and 32 cynomolgus macaques. Reads were then assembled to the rhesus genome and annotated using predicted and experimentally verified mRNA sequences.
Results: The number of reads per animal ranged from approximately 1 to 10 million (median 6.5 million) and alignment to the rhesus genome ranged from 91.8% to 95.6% (median 94.3%). Of the 373 GPCRs targeted, 354 had complete coverage across the gene. Median coverage for the individual animals was 99.75%. Over 24,000 SNPs were identified including over 14,000 non-synonymous and over 9,500 synonymous SNPs. As predicted, the majority of SNPs are singletons, though ~1750 non-synonymous and ~2900 synonymous SNPs were identified in multiple individuals. Among the non-synonymous SNPs identified in multiple individuals 14 were in the opioid receptors, 36 in the dopamine receptors, 59 in the serotonin receptors, and 2 in the cannabinoid receptors. Bioinformatic and functional characterization of these SNPs and others alongside humans are ongoing.
Conclusions: We have identified a large number of potentially functionally relevant SNPs in genes associated with drug abuse and pharmaceutical efficacy. Elucidating genetic diversity improves the translational validity of models of addiction and furthers drug discovery and modeling of the pharmacogenetic effects observed in humans.
Financial Support: This project was supported by NIH grants: OD011103, AA019688. Additional support provided by the NEPRC Primate Genetics Core.

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EFFECT OF DRONABINOL (ORAL THC) MAINTENANCE ON CANNABIS SELF-ADMINISTRATION.

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Aims: There is a clear need for advancing the treatment of cannabis use disorders. One approach is to identify medications likely to assist in the initiation and/or maintenance of abstinence. Prior research has demonstrated that dronabinol (oral THC) can dose-dependently suppress cannabis withdrawal and reduce the acute effects of smoked cannabis. The present study was conducted to evaluate whether high-dose dronabinol maintenance could reduce cannabis self-administration among dependent users.
Methods: Non-treatment seeking daily cannabis users (N=13) completed a residential research study. They were administered 0mg, 120mg, or 180-240mg dronabinol per day (40-80mg tid) for 12 consecutive days in a counterbalanced order. During each 12-day dronabinol maintenance phase, participants were given the opportunity to self-administer smoked cannabis containing <1% THC (placebo) or 5.7% THC (active) by volume under forced-choice (drug vs. money) or progressive ratio conditions. Under the forced-choice self-administration conditions, the monetary choice alternative ranged from $0.25 to $2.00.
Results: Significant main effects of marijuana dose ($F = 52.2 - 391.5$; $p < .001$) and dronabinol dose ($F = 4.1 - 9.1$; $p < .05$) were observed. Pairwise comparisons indicated that participants self-administered significantly more active cannabis compared with placebo in all conditions as expected. When active cannabis was available, self-administration was significantly reduced during periods of dronabinol maintenance (both doses) compared with periods of placebo maintenance. There was no difference in self administration between the 120mg/day and the 180-240mg/day dose conditions.
Conclusions: This is the first demonstration that dronabinol maintenance can reduce cannabis self-administration in daily cannabis users. Considering that dronabinol has also been shown to reduce withdrawal and the acute effects of smoked cannabis, use of dronabinol or similar cannabinoid agonist medications should continue to be explored as a means of aiding initial abstinence in the treatment of cannabis use disorders.
Financial Support: NIDA grant R01-DA025044

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CHRONIC DISEASE AS A PREDICTOR OF PRESCRIPTION MEDICATION MISUSE: FINDINGS FROM A SELF-REPORT STUDY.

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Aims: Prescription drug misuse has received growing attention in recent years. In 2011, 6.1 million Americans reported non-medical use of prescription drugs in the previous month (SAMHSA, 2012). The present study examines the relationship between prescription drug misuse and chronic health conditions.
Methods: Patients receiving outpatient services at a large urban hospital completed a 15-minute computerized questionnaire on domains including demographics, recent substance use, and health conditions with which they had been diagnosed (e.g., heart disease, high blood pressure, chronic pain, depression, etc.). Prescription misuse was defined as: taking one's own prescription more frequently or at a higher dosage than prescribed, taking someone else's prescription, or obtaining the same prescription from multiple physicians. Logistic regression was used to examine associations between chronic health conditions and self-reported prescription misuse in the past 30 days.
Results: N = 2,695 patients completed the survey. The sample was primarily African-American (71.5%) female (75.6%); 7.5% (n=203) reported recent misuse. The conditions most likely to be associated with prescription misuse were pancreatitis (17.3%), hepatitis (16.3%), and liver disease (14.5%). Compared with patients reporting no chronic conditions, patients having 1-2 chronic conditions were 2.4 [95% CI = 1.2, 4.5] times more likely to report misuse in the past month, while patients with 3-4 conditions were 2.7 [95% CI = 1.4, 5.2] times more likely to report misuse, and patients with 5+ conditions were 3.6 [95% CI = 1.9, 7.0] times more likely to report misuse, ($X2(3)= 19.78$, $p<.001$).
Conclusions: Findings support a link between chronic disease and prescription drug misuse. The likelihood of misuse increases in patients diagnosed with multiple chronic diseases. Primary care providers have a unique opportunity to identify patients at risk for such misuse.
Financial Support: NIDA #1R01DA026091-01

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MEDICAL USE, MEDICAL MISUSE, AND DIVERSION OF OPIOIDS AMONG ADOLESCENTS INVOLVED IN ORGANIZED SPORT.

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Aims: The aim of this study was to assess the prevalence of medical use, medical misuse, and diversion of opioids among adolescents who participated in organized sports. Serious attention must be directed toward this population of adolescents who are at greater risk of injury which may require opioids to control pain. Given the significant increase in high school sport participation and the concomitant rise in prescribing opioids to adolescents over the past two decades, this study focuses attention on a population of adolescents who are at risk for misusing and distributing a highly addictive medication.
Methods: Data for this study were taken from the Secondary Student Life Survey, a longitudinal study funded by the National Institute on Drug Abuse. The sample was from a population of students attending two middle schools and three high schools in the Detroit metropolitan area. A total of 1,540 adolescents participated in all three waves of data collection occurring between 2009 and 2011, with 82% of the baseline sample completing all three waves.
Results: Using a Generalized Estimating Equation to analyze the longitudinal sample, it was found that the odds of being prescribed opioids (AOR=1.88), misusing prescribed opioids (AOR=13.22), and diverting prescribed opioids (AOR=3.68) during this three year period were higher among males that participated in organized sports during each wave of the study (these associations were absent among female participants).
Conclusions: With respect to the associations between participation in organized sports and prescribed use, misuse, and diversion of prescribed opioids, males who continually participated in these activities were at highest risk. The results offer insight in detecting an at-risk population who faces the potential to misuse prescription opioids. More importantly, the findings point to groups of adolescents who are more likely to divert controlled medications, which may put other adolescents at risk to nonmedically use prescription opioids.
Financial Support: Supported by NIDA research grant R01DA024678.

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WEAKER RELATIONSHIPS AMONG SUBSTANCE USE AND NEGATIVE CONSEQUENCES IN A NATIVE-AMERICAN TREATMENT-SEEKING SAMPLE.

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Aims: The robust relationship between substance use and associated negative consequences is well documented. While Native Americans as a whole experience many alcohol-related consequences when they choose to consume alcohol, tribal heterogeneity precludes generalization across all tribes (May & Gossage, 2001). The present study sought to explicate the relationship between recent alcohol consumption and negative consequences in a reservation-based treatment-seeking Native American sample in the Southwest.
Methods: As part of a randomized controlled trial of an adapted version of motivational interviewing and the community reinforcement approach (MICRA) versus treatment as usual (TAU), 76 participants (male 74%) completed a baseline assessment including an adapted version of Addiction Severity Index (ASI; McLellan et al., 1992) and the Inventory of Drug Use Consequences (InDUC-2R; Miller, Tonigan, & Longabaugh, 1995).
Results: Given the heavy drinking style reported in this sample, the reported negative consequences were relatively low overall. Surprisingly, frequency of drinking days (past 30) was unrelated to any of the five InDUC subscales ($r = .15$, $p < .19$) and frequency of binge drinking days (past 30) was only significantly related to one of the five subscales on the InDUC-2R, physical consequences ($r = .23$, $p < .04$). Furthermore, there were no significant gender differences on any of the five InDUC subscales of negative consequences.
Conclusions: The absence of a clear relationship between alcohol consumption and negative consequences is surprising given the binge style of drinking among our sample. Further qualitative research may help elucidate this lack of relationship and inform future substance use interventions meant to decrease health disparities for Native Americans.
Financial Support: Supported by NIDA R01-021672

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CONDITIONED TASTE AVERSION PREDICTS MORPHINE, BUT NOT COCAINE, SELF-ADMINISTRATION: A ROLE OF DRUG AVERSION IN DRUG-TAKING.

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Aims: Drugs of abuse are complex pharmacological compounds that have rewarding and aversive effects, both of which should be taken into account when modeling drug-taking behavior. Drug reward has been well implicated in drug use; however, the role of drug aversion has not been systematically examined. The present studies assessed the ability of conditioned place preferences (CPP) and conditioned taste aversions (CTA) to predict morphine and cocaine self-administration.
Methods: Rats were first trained in a combined CTA/CPP procedure with either morphine (5 mg/kg) or cocaine (20 mg/kg). They were then trained to press a lever for intravenous morphine (0.56 mg/kg) or cocaine (0.75mg/kg). The strength of both CTAs and CPPs was then examined in relation to subsequent drug self-administration.
Results: There was a significant relationship between the magnitude of CTA ($\rho = 0.517$; $p < 0.05$) but not CPP ($\rho = -0.330$; $p > 0.05$) and the number of morphine infusions taken. There was also a significant difference between high and low CTA responders in the number of morphine infusions taken (high < low; $t(12) = -3.493$; $p<0.01$). There was no difference between the high and low CPP responders in the number of morphine infusions ($t(12) = -0.179$; $p > 0.05$). There was no significant relationship between the magnitude of CTA ($\rho = -0.110$; $p>0.05$) or CPP ($\rho = -0.053$; $p > 0.05$) and number of cocaine infusions. There was also no significant difference between high and low CTA responders ($t(12) = 0.833$; $p > 0.05$) or high and low CPP responders ($t(12) = -0.106$; $p > 0.05$) in number of cocaine infusions taken.
Conclusions: The aversive effects of morphine, but not cocaine, predict drug self-administration, suggesting that drug aversion should be taken into account in modeling drug taking. These results also add to the literature showing that opiates and psychostimulants differ on a number of behavioral, physiological and neurochemical measures.
Financial Support: Supported by grants from the Mellon Foundation to AV and ALR and from NIDA grant R01DA008651 to DNK.

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FATTY ACID AMIDE HYDROLASE GENE VARIANT INFLUENCES ACUTE RESPONSES TO COCAINE.

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Aims: The endocannabinoid system mediates the effects of cannabis and influences responses to cocaine. The activities of several endocannabinoid receptor ligands are, in part, terminated by fatty acid amide hydrolase (FAAH). The common variant rs324420 C/A, within the FAAH gene on chromosome 1, codes for a missense substitution (Pro129Thr). The rs324420 AA genotype increases the risk for substance use disorders. We hypothesized that the FAAH Pro129Thr variant would affect cocaine-induced subjective effects.
Methods: Non-treatment seeking cocaine-dependent volunteers received placebo and cocaine (0 and 40 mg, IV; randomized). Visual analog scale (VAS) forms, which were used to rate cocaine-induced subjective effects on a scale from 0 (no effect) to 100 (strongest ever), were completed 15 min before (baseline) and 5, 10, 15, and 20 min after infusions. DNA was genotyped for the FAAH rs324420 variant. Results were corrected for population structure. Data was analyzed using repeated measures ANOVA.
Results: On average, the participants (N=47) were 44 year old black (68%) men (87%) who smoked (94%) 2.2 grams of cocaine per day. There were 18 CC, 14 AC, and 15 AA genotypes. FAAH rs324420 was associated with differential ratings of "Stimulated" ($p = 8.89 \times 10\text{-}6$) and "Good Effects" ($p = 2.70 \times 10\text{-}4$) following cocaine administration.
Conclusions: This study suggests that in cocaine-dependent individuals the variant rs324420, which may lead to increased endocannabinoid levels, influences subjective responses to cocaine. Thus, medications that alter levels or activity of FAAH may decrease the rewarding effects of cocaine and have potential therapeutic efficacy for cocaine dependence.
Financial Support: NIH/NIDA SUPPORT: DA018197 (TRK); DA023624 (RDLG); DA018197 (TFN); DA026120 (DAN). This work was conducted at, and supported by the Michael E. DeBakey VA Medical Center, Houston, TX.

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ARREST FOR VIOLENT OFFENSES IN EARLY ADULTHOOD: PREDICTIONS FROM PRENATAL AND ADOLESCENT COCAINE EXPOSURE.

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Aims: To estimate single and combined effects of prenatal cocaine exposure (PCE) and adolescent cocaine exposure (ACE) on occurrence of arrest for violent offenses in early adulthood.
Methods: Data are from a large, well-retained urban, low socioeconomic status sample of 378 full-term African American infants (195 PCE, 183 non-PCE) who were enrolled prospectively at birth in the longitudinal Miami Prenatal Cocaine Study (MPCS) and were currently residing in Florida at the 18/19 year follow-up visit. PCE was assessed via maternal self-report and toxicology assays in maternal urine and infant urine and meconium. ACE was assessed by toxicology assays only. Arrests for violent offenses in early adulthood were based on search of official Florida arrest records. Estimates are presented, with and without consideration of other sources of variation such as prenatal exposure to alcohol, marijuana, and tobacco, and caregiver arrest record.
Results: Estimates from stratified analyses found arrests for violent offenses in early adulthood for an estimated 22% of males with neither PCE nor ACE versus 46% for males with both PCE and ACE ($p<0.05$); corresponding estimates for females were 14% and 23%, respectively ($p>0.05$). The male risk ratio for combined PCE and ACE associated occurrence of arrest for violent offenses of approximately 2.0 ($p<0.05$) did not change appreciably with covariate adjustments for other prenatal drug exposures and caregiver arrest record.
Conclusions: PCE combined with ACE was robustly predictive of arrests for violent offenses, especially in young adult males. Limitations of adolescent self-report are constrained via focus on toxicological assays and official arrest statistics.
Financial Support: NIH National Institute on Drug Abuse and Office of Research on Women's Health (ORWH): R01DA006556 (ESB); P50DA024584(ESB); P50DA024584-S4 (ESB; DCV); K01DA016720 (VHA); K05DA15799 (JCA)

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COMPARING SELF REPORT AND URINE DRUG SCREENS FOR SUBSTANCE USE.

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Aims: Assessing drug use often relies upon self-report measures. However, underreporting consumption of drugs is common and may be due to the stigma associated with this behavior. This study examined the agreement between patients' reported drug use and their urine drug test results.
Methods: Participants were 302 female (67%) and male (33%) patients receiving services from an urban university hospital who reported drug or heavy alcohol use on a computerized screening survey. Participants completed the Timeline Follow-Back (Sobell et al., 1996) interview with a staff member to assess frequency of drug use (i.e. marijuana, cocaine, heroin, hallucinogens, speed) during the previous thirty day period. They were also asked to report medications currently prescribed to them and to provide a urine sample. The current analysis excluded participants who reported a current prescription for opioids or benzodiazepines.
Results: Participants were predominantly African-Americans (78%), in their mid-forties (mean=44.2, SD=11.5) with a high school education (62%). Forty-four percent of the sample reported recent drug use in the past thirty days, with a mean use of 12 days (SD= 11.4). Marijuana use was most frequent (69%), followed by cocaine (22%). While half of the sample (51%) tested positive for at least one drug, only two-thirds (66%) of those testing positive self-reported recent drug use in the face-to-face interview. There was a significant relationship between participants' reporting their drug use and the type of drug they tested positive for ($X^2 = 9.85$, $p < .007$). Marijuana users were likelier to have agreement between their self-reported use and positive urine test ($X^2 = 60.94$, $p < .001$), followed by cocaine users ($X^2 = 96.17$, $p < .001$), followed by opiate users ($X^2 = 3.67$, ns).
Conclusions: While overall rate of self-reported drug use were lower than those found by urine drug toxicology, the relationships varied with different patterns for cocaine and marijuana than for opiates.
Financial Support: Research supported by the National Institute on Drug Abuse #1R01DA026091-01.

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WITHDRAWN

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USE OF SYNTHETIC DRUGS AMONG PEOPLE WHO INJECT DRUGS IN SAN DIEGO, CA.

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Aims: Public concern over hospitalizations and poisonings attributed to the use of synthetic cathinones (SC; aka "Bath Salts") and THC homologues (TH; e.g., Spice) have resulted in calls for a greater understanding of the epidemiology of their use.
Methods: From June to October 2012 we surveyed persons who inject drugs (PWID) in San Diego about their lifetime use of SC and TH, as part of an ongoing cohort study. We hypothesized that users of SC and TH would display different demographic and drug use profiles.
Results: Among 221 PWID enrolled to date, 15 (7%) and 69 (31%) reported lifetime use of SC and TH, respectively. Twenty percent of TH users also used SC. SC users were slightly younger and more frequently male and white than TH users. Most first used these drugs within the past year. Compared to non-users, SC users and TH users were significantly younger ($p<0.01$) and more likely to report recent use of other drugs including: marijuana (TH only, $p<0.01$), drug mixtures ($p<0.05$), methamphetamine (TH only; $p< 0.05$), hallucinogens or inhalants ($p<0.05$), club drugs ($p<0.05$), and prescription drugs ($p<0.05$). Curiosity was the main reason for use of synthetic drugs (60% SC, 47% TH); other reasons included wanting to avoid testing positive on a drug test (13% SC, 12% TH), greater availability (13% SC, 8% TH), and as a substitute for marijuana (9% TH only). Most were obtained from friends or purchased at gas stations/convenience stores; none reported obtaining the drugs via the internet. No SC users and one TH user reported hospitalization due to using the drug. Two-thirds of SC users think SC is legal and 72% of TH users think TH is legal.
Conclusions: Findings suggest that over one-third of surveyed PWIDs have used emerging synthetic drugs. Users may be characterized by different demographic and drug use profiles than other PWIDs and have largely obtained drugs through social contacts or convenience stores. Despite CA legislation passed in 2011 banning these drugs, most users think they are legal. Users may require interventions tailored to use of multiple substances.
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ATTENUATION OF RATE-FREQUENCY INTRACRANIAL SELF-STIMULATION DURING NICOTINE WITHDRAWAL IN RATS.

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Aims: Affective consequences of nicotine withdrawal are known to influence the high rate of recidivism in abstinent smokers. In humans, this affective withdrawal syndrome consists of anxiety, anhedonia, irritability, and other symptoms suggestive of decrements in brain reward function. In laboratory animals, drug effects on reward can be examined using intracranial self-stimulation (ICSS). Whereas many abused drugs facilitate responding reinforced by direct electrical stimulation of the mesolimbic dopaminergic reward pathway, several studies have indicated that withdrawal from a chronically administered drug (e.g., nicotine) results in an attenuation of ICSS-maintained responding. The goal of the present study was to model reward-related deficits during nicotine withdrawal using a rate-frequency ICSS procedure and examine their duration.
Methods: Male Sprague Dawley rats were implanted with electrodes aimed at the medial forebrain bundle and trained in a rate-frequency ICSS paradigm, where they responded through a series of decreasing stimulation frequencies. Once behavior stabilized, subjects were implanted with osmotic minipumps containing either 3 mg/kg/day nicotine or saline (N=8/group). Mecamylamine-precipitated withdrawal and spontaneous withdrawal tests were conducted 7 and 12-15 days after minipump implant, respectively. Withdrawal effects were operationally defined as rightward shifts in ICSS rate-frequency curves and increases in thresholds relative to baseline.
Results: In rats receiving nicotine, mecamylamine produced a rightward shift in the rate-frequency response curve and a trend towards increased reward thresholds. Significant spontaneous withdrawal effects were seen at various times during the first three days of nicotine withdrawal. Thresholds were unaltered during any withdrawal tests in the saline group.
Conclusions: These results indicate that under these conditions, nicotine withdrawal decreases brain reward function over the course of several days, with maximal effects observed approximately 2 and 24 h post-withdrawal.
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CONCEPT MAPPING TO GENERATE ITEMS FOR THE PATIENT OPIOID EDUCATION MEASURE (POEM).

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Aims: Although there are screening tools to aid clinicians in assessing the risk of opioid misuse, an instrument to assess opioid-related knowledge in patients is not currently available. The aim of this study was to report the preliminary development of the POEM to assess patients' understanding of opioid safety information.
Methods: Concept mapping was used to guide POEM development. Fourteen clinicians caring for patients with chronic pain participated in the brainstorming phase and responded to the following focus prompt: "Thinking as broadly as possible, please list specific need-to-know information for patients prescribed opioids." Once statements (n=388) from the brainstorming phase were collected, duplicate items were removed. Thirty-seven individuals (primary care physicians, n=24; pain specialists, n=9; pharmacists, n=2; clinical psychologist, n=1; medical librarian, n=1) completed a "free" sort of 131 non-duplicate statements based on similarity and rated each statement on a 5-point importance scale. Data were entered and analyzed using Concept Systems® software.
Results: Clinicians generated an average of 24.1±7.3 statements. Concept mapping identified 7 clusters addressing knowledge and expectations associated with opioid use, including: (1) medicolegal issues, (2) prescribing policies, (3) safe use and handling, (4) expected outcomes, (5) side effects, (6) pharmacology, and (7) warnings. A total of 48 statements (36.6%) had an importance rating of ≥4.00 and were included within the POEM.
Conclusions: The POEM shows promise in allowing clinicians to quickly pinpoint patients' knowledge-related gaps related to opioid therapy. Further validity, reliability, and readability testing of the POEM is pending.
Financial Support: Supported by a grant from Purdue Pharma L.P.

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NASAL NALOXONE RESCUE KITS IN AN EMERGENCY DEPARTMENT OVERDOSE EDUCATION PROGRAM.

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Aims: Due to increasing opioid-related overdoses (OD), our emergency department (ED) provided OD education (OE) to patients at risk or likely to witness an OD. OE included how to prevent, recognize, and respond to ODs. We hypothesized that OE with nasal naloxone rescue kits (OEN) compared to OE only was associated with 1) non-fatal OD, 2) using illicit opioids, 3) engaging in methadone or buprenorphine (agonist) treatment and 4) responding appropriately to a witnessed OD.
Methods: In this retrospective cohort, we used hospital records to telephone survey ED patients who had previously received OE between January 2011 and February 2012. Data included self-reported and witnessed ODs since OE, 30-day substance use, and witnessed OD response actions (calling 911, rescue breathing, administering naloxone). We used chi-square tests to compare OEN to OE only groups.
Results: Of 415 ED patients who received OD education, we contacted 51 (12%), a mean of 11.8 months after their ED visit. Of the 73% (37/51) in the OEN group, 76% (28/37) received naloxone kits in the ED and 24% (9/37) received them in detox, needle exchange, or methadone programs. When we compared OEN and OE only groups, 19% vs. 29% self-reported an OD (p=0.45), 36% vs. 35% reported illicit opioid use (p=1.0) and 49% vs. 36% reported agonist treatment (p=0.53), respectively. Among the 53% (27/51) who witnessed an OD, 84% (16/19) in the OEN group vs. 38% (3/8)in the OE only group responded to the OD by calling 911, rescue breathing or administering naloxone (p=0.03).
Conclusions: In this first study of an ED-based OD prevention intervention, a higher proportion of patients equipped with naloxone than those not equipped responded to an OD. No significant differences were detected in self-reported ODs, illicit opioid use, or agonist treatment. OD education including naloxone is a promising intervention that warrants larger, systematic prospective studies.
Financial Support: Boston University Evans Medical Foundation faculty award

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GENDER-BASED VIOLENCE, PSYCHOPATHOLOGY AND SUBSTANCE USE DISORDERS IN A NATIONAL SAMPLE OF WOMEN.

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Aims: Gender-based violence (GBV; physical/sexual violence, stalking) is an important public health issue (World Health Organization, 2005). Although exposure to more types of GBV is associated with increased risk for psychopathology and substance use disorders (SUDs) (Rees et al., 2011), and experiencing violence early in life (versus later) is associated with poorer outcomes (Manly et al., 2001), no studies have compared these factors. We examined whether cumulative GBV exposure or earlier GBV exposure was a stronger relative predictor of psychopathology and SUDs.
Methods: Participants were 20,089 women from wave 2 (2004-2005) of the National Survey of Alcohol and Related Conditions (NESARC). GBV included sexual or physical violence and stalking. Psychopathology and SUDs were assessed with the reliable and valid AUDADIS (Grant et al., 2005).
Results: One-quarter (n=5,086) of women reported any lifetime GBV: 9.3% (n=1856) 1 type, 12.5% (n=2489) 2 types, and 3.6% (n=725) all 3 types. In adjusted models, those with GBV were 2.2 to 6.1 times more likely to report psychopathology and 2.3 to 6.7 times more likely to report SUDs. GBV was associated with particularly elevated risk for posttraumatic stress disorder (AOR =6.07, 95% CI=6.06,6.075) and borderline personality disorder (AOR=6.14, 95% CI=6.13,6.15) as well as with less common SUDs including amphetamine (AOR=5.26, 95% CI=5.24,5.26) and inhalant (AOR=6.70, 95% CI=6.62,6.78) use disorders. Odds of reporting psychopathology and SUDs were 1.7 to 4.8 times higher among those reporting 3 (versus 2) types of GBV and 1.6 to 3.0 times higher among those first exposed to GBV between ages 12-18 (versus age 19 or older).
Conclusions: Any GBV was strongly related to psychopathology characterized by emotion dysregulation as well as SUDs involving more "deviant" substances. Cumulative GBV exposure was a stronger relative predictor of negative outcomes than was earlier exposure to GBV. However, GBV during adolescence also was associated with risk for psychopathology and SUDs, highlighting a possible critical period for violence exposure.
Financial Support: T32DA031099

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MAPIT: DEVELOPMENT OF A COMPUTER-BASED INTERVENTION TARGETING SUBSTANCE ABUSE TREATMENT IN THE CRIMINAL JUSTICE SYSTEM.

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Aims: Aim: Although drug and alcohol treatment are common mandates in the U.S. criminal justice system, only a minority of clients actually initiate treatment. This paper describes the rationale behind and development of a two-session, computer-based intervention to increase motivation for substance abuse treatment among clients with court-ordered treatment requirements.
Methods: MAPIT (Motivational Assessment Program to Initiate Treatment) draws from motivational interviewing, the Extended Parallel Process Model, and Social Cognitive Theory. The first session (completed near the start of probation) targets motivation to complete probation, to make changes in substance use (including treatment initiation), and to obtain HIV testing and care. The second session (completed approximately 30 days after session 1) focuses on goal setting, coping strategies, and social support. Both sessions include an automated reminder feature, where clients can generate emails or mobile texts to remind them of their goals. This paper also describes how the program is able to provide personal responses and suggestions using theory-based algorithms and a text-to-speech engine. MAPIT is being tested in a randomized treatment trial in two large U.S. probation agencies. Primary outcomes include engagement and participation in substance abuse treatment; secondary outcomes include drug and alcohol use, criminal behavior, and HIV testing and care.
Conclusions: MAPIT addresses the struggle of many probation agencies to maximize client involvement in treatment, in a way that is cost effective and compatible with the existing service delivery system.
Financial Support: Supported by a grant from the National Institute on Drug Abuse (R01 DA029010-01; PI: Walters)

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DOES PREGNANCY ALTER THE ACTIVITY OF BABOON (PAPIO CYNOCEPHALUS) HEPATIC CYTOCHROME P450 2B IN THE BIOTRANSFORMATION OF BUPROPION?

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Aims: CYP2B6 is the major human hepatic enzyme involved in the biotransformation of bupropion (BUP) to the pharmacologically active metabolite hydroxybupropion (OH-BUP), and the effect of pregnancy on the activity of this enzyme is unclear. Recent in vitro data obtained in our laboratory revealed similarities between baboons and humans in the biotransformation of BUP by both hepatic and placental microsomes as well as that the in vitro hydroxylation of BUP in baboons is catalyzed by CYP2B. These data validated, in part, the use of baboons to study BUP biotransformation during pregnancy. The aim of this investigation is to determine whether the activity of baboon hepatic CYP2B changes with pregnancy and during gestation.
Methods: Pregnant baboons (n=5) received single intravenous (i. v.) bolus dose of BUP hydrochloride (1.0 mg/kg) at gestational age of 94-108 days (middle term), 142-156 days (late term) and 6 weeks post partum, respectively. Blood samples were collected for 72 hours following the administration of each dose of BUP. The concentration of BUP and OH-BUP in plasma was determined using an LC-MS/MS method. The in vivo activity of baboon CYP2B was determined by the ratio of AUC OH-BUP vs. AUC BUP.
Results: There is wide inter-individual variability in the biotransformation of bupropion between baboons. The mean of the pharmacokinetics parameters for BUP and OH-BUP did not reveal differences neither during gestation nor postpartum. In addition, the mean AUC OH-BUP vs AUC BUP values determined through gestation were not significantly different from the postpartum value.
Conclusions: The physiological changes associated with the onset of pregnancy did not affect the activity of baboon hepatic CYP2B in the biotransformation of bupropion.
Financial Support: This work was supported by a NIDA grant RO1DA024094 to TN.

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QUANTITATIVE REVIEW OF PSYCHOSOCIAL AND ETHICAL CONTENTS OF HOME DRUG TESTING FOR PARENTS ON THE INTERNET.

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Aims: We quantitatively and systematically reviewed websites that marketed home drug testing kits intended for parents' use.
Methods: We analyzed the psychosocial and ethical contents on these websites using a checklist that we developed and was reviewed by pediatric and behavioral professionals in the field of substance abuse. We identified eight websites that were within the first 50 websites listed in at least two out of four search engines. We checked correspondence between our checklist items and information on each website and where each piece of information was found within each site.
Results: We found that six out of eight websites covered less than half the checklist items (mean ± SEM: 46 ± 8%), and six out of eight websites had more information listed on the webpages that required two or more mouse clicks to reach or on blogs or videos. Six out of eight websites had Parent-related webpages and links, and information under these links covered on average 38 ± 7% of the checklist items. The websites that directly sold home drug testing products (n = 5) covered more of the checklist contents than those that did not directly sell such products (53 ± 11 vs. 35 ± 8%).
Conclusions: The psychosocial and ethical contents of the reviewed websites were relatively poor. Psychosocial and ethical professional guidelines for home drug testing are on demand to protect interested parents and their children from potential unintended psychological, medical, and societal consequences.
Financial Support: All phases of this study were supported by an NIH grant, 5P50DA027841-03.

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EFFECTS OF AMPHETAMINE ON RETRIEVAL OF MEMORY FOR EMOTIONAL STIMULI.

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Aims: Drugs of abuse have been shown to affect memory in both animals and humans. However, little is known about drug effects specifically on emotional memory in humans. Stimulant drugs increase positive mood, and as such it is possible that they could preferentially enhance either encoding or retrieval memory for positive emotional stimuli. In this study we investigated the effects of d-amphetamine (AMP) on retrieval of memory for emotional material in humans. We hypothesized that AMP would enhance retrieval of emotional material, particularly for positive emotional stimuli, possibly through its effects on mood.
Methods: Participants attended an encoding session in which they viewed standardized positive, neutral, and negative pictures from the International Affective Picture System (IAPS; Lang et al, 1999). Exactly 48 hours later they attended a retrieval session testing their memory of these stimuli. A between-subject design was utilized in which participants were randomly assigned to receive either AMP (20mg) or placebo (PL) during encoding and either AMP or PL during retrieval.
Results: The results presented here are limited to the AMP or PL at retrieval. Data collection is currently ongoing, and to date 22 participants have received AMP in the retrieval session and 13 participants have received PL. Preliminary results show that, regardless of drug administered at encoding, participants receiving AMP at retrieval showed enhanced memory for studied items (p=.036), as well as increased false memory (p=.019), but thus far these effects are not specific to emotional stimuli.
Conclusions: As data collection progresses we will test whether AMP preferentially alters memory for positive stimuli, and whether memory is related to subjective mood response to AMP. We hypothesize that greater AMP-induced positive mood will be associated with preferential memory for positive stimuli, thus providing a potential mechanism through which AMP effects on memory may promote further use.
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MARIJUANA USERS' PERCEPTIONS OF HEALTH RESEARCH.

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Aims: To compare perceptions of research among 1,007 self-reported marijuana (MJ) users to 1,159 non-MJ users identified through HealthStreet, a community-engaged research model.
Methods: Community Health Workers (CHWs) from HealthStreet-Gainesville conduct brief health assessments with community members in a variety of settings. Based on health needs, CHWs immediately provide links to medical and social services, and relevant health research. Data collected from these assessments were analyzed using SAS v. 9.2.
Results: As of December, 2,166 community members have completed health assessments, and 46% reported lifetime use of MJ use. Sixty-four% of participants were African-Americans. As compared to non-MJ, MJ users were as likely to report past history of enrollment, willingness to take medicine, and willingness to participate in health research studies for free. MJ users were significantly more willing to provide a blood or genetic sample, stay overnight in a hospital, and to use medical equipment. They were significantly more interested in research participation overall.
Conclusions: These findings signify an important area of research in the era of the CTSA, and indicate novel approaches to reduce research barriers for drug users around the world.
Financial Support: Dr. Linda Cottler is the Principal Investigator (PI), and Dr. Catherine Striley is the Co-PI on this research supported by NIH NIDA and NIAAA. This abstract is sponsored by Dr. Linda Cottler, senior author on this abstract, who is a Fellow Member of the College on Problems of Drug Dependence.

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INCREASED MYELIN PROTEIN EXPRESSION WITHIN THE VENTROMEDIAL PREFRONTAL CORTEX FOLLOWING EXTENDED ACCESS TO COCAINE SELF-ADMINISTRATION IN ADULT MALE RATS.

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Aims: Chronic cocaine abuse in humans results in reduced white matter and expression of myelin proteins in the frontal cortex, which may contribute to maladaptive executive processing in addiction. As little is known regarding the nature of white matter volume loss following cocaine abuse, specifically whether this loss is related to loss of myelin, the present study examined for changes in the expression of myelin proteins within the ventromedial prefrontal cortex (vmPFC) of rats during short- and long-term withdrawal from a history of long-access cocaine self-administration.
Methods: Groups of adult male rats (n=10-13/grp) were trained to lever-press for 0.25 mg/infusion of cocaine or saline during 10 daily, 6-hr sessions. At 3 or 30 days following the last self-administration session, the vmPFC was dissected out and subsequently, processed by immunoblotting for various myelin proteins.
Results: Compared to saline controls, cocaine experienced rats exhibited early and persistent increases in protein expression within the vmPFC as indicated by significant main effects of IV Treatment for myelin basic protein (MBP; $p=0.047$), myelin-oligodendrocyte glycoprotein (MOG; $p=0.050$), proteolipid protein (PLP; $p<0.000$), and claudin-11 ($p=0.046$), with a trend towards significance for 2', 3'-cyclic nucleotide 3'-phosphodiesterase (CNP; $p=0.071$).
Conclusions: It was hypothesized that cocaine experience would produce a decrease in myelin protein expression within the vmPFC, based on previous human imaging and post-mortem microarray data. However, our results show an increase in myelin protein expression following cocaine. While these results appear contradictory, the stability of the myelin sheath is particularly sensitive to the relative proportion of myelin proteins. Both decreases and increases in MBP and PLP can lead to a loss of sheath compaction, and ultimately demyelination. Therefore, an increase in myelin proteins could account for the decrease in white matter volume seen consistently in human cocaine addicts.
Financial Support: NIDA grant DA024038 to KKS

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SELF-GENERATION ENHANCES VERBAL RECALL IN HIV-INFECTED STIMULANT USERS.

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Aims: Stimulant dependence is often associated with moderate deficits in verbal learning and memory that interfere with everyday functioning, but few studies have sought to remediate such deficits. The present study explored the efficacy of a self-generation technique, which enhances new learning via elaborated encoding mechanisms, in HIV-infected stimulant users.
Methods: Participants included 18 HIV+ adults with histories of stimulant dependence and 15 HIV- individuals with no substance dependence history, who learned paired word associates through either self-generated or didactic encoding. In the didactic condition, participants received completed word pairs that they were instructed to read aloud. In the self-generation condition, participants received the first word, but the second word was self-generated based on its first letter and the given relationship between the words (e.g., "synonym"). The primary dependent variables of interest were the 20-minute delayed free recall scores from the self-generation and didactic conditions.
Results: A mixed-factor ANOVA revealed main effects of group status ($p=0.004$) and encoding condition ($p<0.001$), but no interaction between group status and encoding condition ($p>0.10$). Further exploration of these omnibus effects showed that HIV+ stimulant users recalled fewer words overall compared to their healthy counterparts, and that both groups recalled significantly more words learned in the self-generation condition. Of note, HIV-infected stimulant users recalled significantly fewer words compared to the healthy comparison group in the didactic condition ($p=0.005$; $d=-1.19$), but normalized their performance with the self-generation strategy ($p>0.10$; $d=0.20$).
Conclusions: Findings suggest that self-generation may improve verbal recall in HIV-infected stimulant users and may therefore be an appropriate and potentially effective cognitive rehabilitation tool in this population.
Financial Support: NIDA, NIMH

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ABUSE POTENTIAL ASSESSMENT OF NOVEL OPIOID ANALGESIC NKTR-181: IMPLICATIONS FOR LABELING AND SCHEDULING.

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Aims: Discuss challenges to opioid development when early data suggest the possibility of less restrictive scheduling than CII. This will be illustrated by initial findings for NKTR-181. NKTR-181 is a new molecule intended to provide analgesic efficacy of prototypic mu-opioids but with reduced respiratory depression, sedation and abuse potential. Mu-opioid activity of NKTR-181 is retained in a morphinan core to which polymers are covalently bound resulting in slower and lower brain penetration upon oral or parenteral administration to animals than prototypic opioids. Morphinans are placed in Schedule II during development and can only be rescheduled if the abuse potential assessment by FDA (during review of the New Drug Application) warrants less restrictive scheduling. This regulatory challenge is not unique to NKTR-181 but data concerning NKTR-181 will be included to support the commentary. Although oral NKTR-181 is readily absorbed, time course of pupil constriction lags drug plasma appearance 2 to 3 hr, consistent with a reduced rate of CNS uptake. These effects are maintained after repeat administration with no evidence of tolerance. Nonclinical studies suggest mu-opioid CNS effects are of substantially lower potency for NKTR-181 compared to other opioids with mixed findings across models, e.g., NKTR-181 produced dose-related generalization similar to prototypic opioids at doses many times analgesic doses but with significantly reduced reinforcing effects. Opioid-like side-effects linked with abuse potential (e.g., "dreamy", "sleepy", "high") were not reported in healthy volunteers at expected therapeutic doses with central effects no different than placebo.
Conclusions: A preliminary 8-Factor analysis of NKTR-181 suggests lower abuse potential than prototypic Schedule II opioids. How FDA addresses this challenge to drug development and scheduling will have implications for other drugs in development.
Financial Support: Nektar

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BRIEF SCREENING FOR ALCOHOL AND DRUG PROBLEMS AMONG PRISONERS.

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Aims: Although drug and alcohol abuse rates are high among prisoners, these problems often go undetected, which represent lost treatment opportunities. Brief, no-cost screening instruments can be used to efficiently identify individuals who could be further assessed and who may benefit from treatment. The purpose of this study is to examine the feasibility of using the Alcohol Use Disorders Identification Test (AUDIT) as a brief screener for alcohol use among prisoners and whether it can identify other drug problems.
Methods: The AUDIT and the NIDA-modified Alcohol, Smoking, Substance Involvement Screening Test (NM-ASSIST) were administered to 382 prisoners in four Kentucky state prisons who were approaching release and consented to participate in NIDA Criminal Justice Drug Abuse Treatment Studies (CJDATS 2) cooperative agreement protocols. Participants were divided into two groups based on whether they screened positive (n= 189) or negative (n= 193) on the AUDIT. NM-ASSIST Substance Involvement (SI) scores were calculated for each of the nine drugs measured by the NM-ASSIST and compared between AUDIT groups.
Results: No significant differences in age, race, or rurality for AUDIT groups were found, but the AUDIT positive group had a significantly higher percentage of males (73.0% vs. 61.5%). ANCOVAs, controlling for gender, found significantly higher SI scores ($p < .05$) for the AUDIT positive group for cannabis (15.0 vs. 10.3), cocaine (15.3 vs. 8.0), prescription stimulants (5.0 vs. 1.9), inhalants (0.6 vs. 0.2), sedatives (10.7 vs. 5.7), hallucinogens (1.1 vs. 0.5), and prescription opiates (15.6 vs. 11.1). No differences were found for SI scores for methamphetamine or street opioids.
Conclusions: Findings suggest that prisoners who screen positive on the AUDIT have higher drug risk than those who screen negative, which suggests that the AUDIT may be an indirect screening for other substance problems. The majority of SI scores fell in the moderate risk range (4 to 26), suggesting that prisoners have drug risk for multiple drugs.
Financial Support: CJDATS 2 is funded by NIDA in collaboration with SAMSHA and DOJ.

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ASSOCIATION OF THE A335G POLYMORPHISM WITH STRIATAL DOPAMINE D2/3 RECEPTOR AVAILABILITY IN HEALTHY MEN AND WOMEN.

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Aims: Dopamine release (DAR) in the ventral striatum (vS) plays a key role in drug reward, craving and relapse. Recently, the minor G-allele of A335G (rs1799971, previously A118G) single nucleotide polymorphism (SNP) has been associated with greater DAR in response to alcohol administration and tobacco smoking in male social drinkers and smokers, respectively. This study examined whether the A335G SNP influenced dopamine D2/3 receptor availability and DAR in response to amphetamine (AMPH) administration in 18-30 year old healthy normal men and women.

Methods: Each subject completed two 90-min positron emission tomography (PET) scans with ^{11}C-raclopride (RAC). Five min before injection of RAC, an intravenous injection of saline (baseline, scan 1) or 0.3 mg/kg AMPH (scan 2) was administered. Non-displaceable binding potential (BP_{ND}) of RAC was determined using cerebellum as the reference region. DAR was estimated as the percent change in BP_{ND} between the baseline and AMPH scans. Men (n=51) and women (n=37) were analyzed separately via multiple regressions with genetic ancestral population as a covariate. We grouped carriers of the G allele (AG/GG) together.

Results: In the striatum, baseline BP_{ND} was significantly greater in carriers of the G allele when compared to noncarriers in both men ($p=<0.05$) and women ($p<0.05$). In the vS, baseline BP_{ND} was significantly greater in G-carriers vs. noncarriers in men ($p<0.05$), but not in women. There were no significant genotype differences in AMPH-induced DAR in the striatum or the vS for either gender.

Conclusions: These data indicate that A335G genotype did not predict the magnitude of DAR in normal healthy subjects, but was associated with baseline differences in D2/3 availability in the vS (males only), and in the whole striatum (both genders).

Financial Support: R01 AA012837, R01 AA010158

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MOTIVE-SPECIFIC DIFFERENCES IN NONMEDICAL USE OF PRESCRIPTION PAIN RELIEVERS AMONG ADOLESCENTS.

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Aims: Findings from a growing body of research suggest that pain relief motivates a substantial proportion of adolescents who use prescription pain relievers for nonmedical purposes (McCabe, et al., 2009). But it remains unclear if differences exist between adolescents who are currently engaged in the nonmedical use of prescription pain relievers (NMUPPR) for the purpose of "relieving pain" [PR] and adolescents who are currently engaged in the NMUPPR for the purpose of "getting buzzed, high, stoned, or wasted" [BHSW]. The aim of this study was to examine these two motive-specific differences in the NMUPPR among adolescents.

Methods: Data were collected from a sample of 4,178 students in grades 9 -12 enrolled in five high schools using a cross-sectional survey research design. Bivariate analyses using χ^2 were used to examine demographics and patterns of NMUPPR between adolescents who reported using a prescription pain reliever for PR and those who reported using to get BHSW.

Results: Data were collected from a sample of 4,178 students in grades 9 -12 enrolled in five high schools using a cross-sectional survey research design. Bivariate analyses using χ^2 were used to examine demographics and patterns of NMUPPR between adolescents who reported using a prescription pain reliever for PR and those who reported using to get BHSW.

Conclusions: NMUPPR among adolescents differed for users motivated by PR than those motivated by getting BHSW. Findings have implications for adolescents who need medically supervised pain management and those who abuse prescription pain relievers.

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SEX DIFFERENCES IN VA PATIENTS WITH CHRONIC PAIN.

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Aims: Despite a growing number of women seeking care in the VA, little is known about the pain care they receive. This study sought to determine if sex differences are present in chronic pain care. This was a retrospective cohort study using administrative data of 17,583 patients with chronic non-cancer pain.

Methods: Multivariate logistic regression assessed sex differences in primary care utilization, receipt of chronic opioid therapy, visits to emergency departments, and physical therapy referral.

Results: Compared to male veterans, female veterans were more often diagnosed with two or more pain conditions. After adjustment for demographic characteristics, pain diagnoses, mental health diagnoses, substance use disorders, and medical comorbidity, women had lower odds of being prescribed chronic opioid therapy (AOR 0.67, 95% CI 0.58-0.78), greater odds of visiting an emergency department for a pain-related complaint (AOR 1.40, 95% CI 1.18-1.65), and greater odds of receiving physical therapy (AOR 1.19, 95% CI 1.05-1.33). Primary care utilization was not significantly different between sexes.

Conclusions: Sex differences are present in the care female veterans receive for chronic pain. Further research is necessary to understand the etiology of the observed differences and their associations with clinical outcomes.

Financial Support: This study was supported in part by award K23DA023467 from the National Institute of Drug Abuse to Dr. Morasco. The Oregon Clinical and Translational Research Institute (OCTRI), grant number UL1 RR024140 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH) also supported this study. Dr. Weimer's time was supported by the Samuel F. Wise Trust.

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WHO BENEFITS FROM MORE INTENSIVE COUNSELING FOR PRESCRIPTION OPIOID DEPENDENCE?

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Aims: The 10-site Prescription Opioid Addiction Treatment Study, conducted as part of the NIDA Clinical Trials Network, examined different lengths of buprenorphine-naloxone (bup-nx) treatment plus medical management, with or without additional counseling, for patients dependent upon prescription opioids. Among patients (N=360) receiving 12 weeks of bup-nx stabilization, 49% achieved a successful opioid use outcome, regardless of counseling condition. The aim of the current study is to consider whether counseling in addition to medical management was related to successful outcomes among those patients with more severe addiction problems.

Methods: A 2-phase adaptive treatment research design examined outcomes during 1) a 4-week taper and 2) 12-week bup-nx stabilization. Successful outcome was defined as abstinence in week 12 of Phase 2 (the last week of bup-nx stabilization) and ≥2 of the previous 3 weeks. High severity was defined as worse ASI drug severity score, lifetime heroin use, or chronic pain.

Results: Logistic regression models showed that patients who had used heroin were more likely to have unsuccessful outcomes (OR=1.85, $p<.02$). ASI drug severity score and chronic pain were not associated with outcome. Receipt of counseling was not significant. However, among those who attended ≥60% of counseling sessions (our a priori definition of adequate dose), the interaction effect of heroin on the association between counseling treatment and outcome was significant: among heroin users, those in counseling were more likely to succeed (66% vs. 36%, $p<.05$); this association was not significant among non-heroin users.

Conclusions: Among patients with prescription opioid dependence who attended most assigned counseling sessions, counseling was associated with improved outcomes only for patients with a history of heroin use.

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LITERATURE REVIEW OF SUBSTANCE ABUSE "TREATMENT AS USUAL" FOR PSYCHOSOCIAL INTERVENTIONS.

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Aims: Considerable progress has been made in the past 15 years towards empirically validating and implementing psychosocial interventions for substance use disorders. An important part of this endeavor is continual documentation of standard practice, or "treatment as usual" (TAU). This documentation is important in order to better understand the complex nature of real-world practice, monitor progress of evidence-based treatment implementation, dovetail implementation efforts with existing practices, and conduct and interpret clinical trials in which TAU groups are used as controls. Historically, little attention has been paid to in-depth examination of TAU, leading some researchers to refer to it as the "black box" of substance abuse treatment. In recent years, however, researchers have increasingly documented TAU, often alongside clinical trials and implementation studies. This presentation is a review of this budding literature, inclusive of data from organizational self-report, clinician self-report, observational studies, and clinical trials (including recently published studies from the NIDA Clinical Trials Network).
Conclusions: Organizations and clinicians are more likely in recent years to report the use of evidence-based practices; however, observations of these practices persistently reveal limited implementation of evidence-based treatments, even among those who report using them and generally across clinicians' education level, licensure status, and theoretical orientation. Although basic motivational interviewing is commonly reported and observed, use of cognitive-behavioral therapy, 12-step facilitation, contingency management, and other evidence-based practices are frequently reported but less frequently observed. Other practices, such as clinician self-disclosure, didactic groups, and unstructured conversation are frequently observed.
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SEX DIFFERENCES IN BRAIN RESPONSES TO SMOKING CUES: A PERFUSION FMRI STUDY.

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Aims: Anecdotal and clinical theories purport that females are more responsive to smoking cues (SCs); however, sex differences in neural responses to SCs remains largely unexplored, as direct comparisons between male and female neural responses to SCs have not been conducted. To address this, the current study examined and directly compared brain responses to SCs among male and female sated-smokers. Based on previous research suggesting greater behavioral and physiological responses to SCs among females relative to males, we hypothesized that females would show greater brain responses to SCs than males in reward-related brain regions.
Methods: Nicotine-dependent 'sated' smokers (N=51, 20 females) participated in a pseudo-continuous arterial spin labeling (pCASL) perfusion functional magnetic resonance imaging (fMRI) during a SC-reactivity experiment consisting of audio/visual video clips of SC or non-SCs (each lasting 10 minutes).
Results: Males exhibited increased medial orbitofrontal cortex and ventral striatum/ventral pallidum responses to SCs compared to non-SCs, and females showed increased medial orbitofrontal cortex responses. Contrary to expectations, direct comparisons between male and female brain responses revealed that males showed greater hippocampal/amygdala activation to SCs relative to non-SCs ($p < .005$, cluster > 54 voxels).
Conclusions: To our knowledge, this is the first neuroimaging study to directly examine sex differences in brain responses to SCs by explicitly comparing male and female brain activity to SCs relative to non-SCs. Findings suggest that sex differences in neural responses to SCs may be related to sex-specific differences in emotional memory-related processes during SC exposure. Future research will examine how menstrual cycle phase may influence sex differences in neural responses to SCs.
Financial Support: This work was funded by National Institutes of Health grants P60-DA-005186 and R21-DA-025882.

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ON-SITE ETHYL GLUCURONIDE IMMUNOASSAY MONITORING OF ALCOHOL USE IN COCAINE-DEPENDENT OUTPATIENTS.

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Aims: This pilot study was conducted to examine the effectiveness of an onsite ethyl glucuronide (EtG) enzyme immunoassay technique for monitoring alcohol use in cocaine-dependent outpatients, a population in whom even social drinking can adversely impact treatment outcomes. Our goal was to examine whether this assay may lend itself to contingency-management (CM) interventions for problem drinking in this population; the test requires only modest technical training, gives results within a short turnaround time, and captures drinking beyond the 6-8 hrs typical of breath tests. We hypothesized that EtG would have acceptable sensitivity and specificity for monitoring problem drinking.
Methods: Eleven participants in a trial of behavioral treatments for cocaine dependence were selected for participation based on self-reported intermittent alcohol use. Self-reported alcohol use, urine EtG levels, and breath alcohol concentrations (BAC) were assessed thrice weekly for 12 weeks. The cutoff for positive EtG results was ≥ 500 ng/mL; for BAC it was ≥ 0.01%.
Results: EtG showed 92% specificity (245/267) in confirming self-reported abstinence over the past two days (recommended window). Sensitivity for detecting self-reported drinking within the prior two days varied by the number of drinks reported: 32% (6/19) for a single drink, 67% (40/60) for 2+ drinks, and 75% (12/16) for binge-level drinking (≥5 drinks for men and ≥ 4 drinks for women). By comparison, BAC showed 100% specificity (267/267) in confirming self-reported abstinence over the past two days, but sensitivity was 0% (0/19) for a single drink; 3% (2/60) at 2+ drinks; and 6% (1/16) for binge-level drinking, significantly below sensitivity of the EtG test ($p < 0.001$).
Conclusions: EtG is likely to be effective for use in CM when urinalysis is conducted at least every other day and the goal is to reduce binge-level drinking, but less helpful where total-abstinence goals may be indicated (e.g., pregnant women).
Financial Support: T32 DA07242
R37 DA09378

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DIFFERENCES IN DRUG USE PATTERNS AND HCV AMONG AFRICAN-AMERICAN ADULT DRUG USERS.

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Aims: The objective of the current study is to examine the differences in drug use patterns and Hepatitis C (HCV) outcomes among a sample of African Americans who use illicit drugs.
Methods: The current study used data from the baseline assessment of the NEURO-II HIV Prevention trial. Participants completed a detailed behavioral assessment of drug use and sexual practices. In addition, they provided blood and urine samples. The present study uses a subset (N= 260) of African Americans from the larger study. Descriptive statistics were used to calculate frequencies, means, and percentages for each variable of interest. Chi-square statistics were conducted by age cohort on demographic variables, drug use behaviors and HCV outcomes. Logistic regression analyses were conducted using drug use and age cohort as predictors of HCV controlling for gender, education, income and marital status.
Results: Patterns of substance use differed by age cohort: older adults reported more crack use (χ^2 (1, N=260) = 8.108, $p < .005$), more injection speedball (χ^2 (1, N= 260) = 7.975, $p<.005$), more injection heroin (χ^2 (1, N=260) = 9.927, $p< .005$), and more nasal cocaine (χ^2 (1, N= 260) = 8.471, $p < .005$). The groups did not differ on nasal speedball, nasal heroin, marijuana, alcohol, or cigarette use. The groups differed on HCV outcomes with more older adults testing positive for HCV at baseline assessment (χ^2 (1, n = 187) = 11.490, p =.001). Logistic regression showed that age cohort and injection drug use both significantly predict HCV outcomes with older adults being almost three times as likely to be positive for HCV (AOR = 2.631, 95% CI = 1.01, 6.81), however age moderation effect was not statistically significant.
Conclusions: With age cohort significantly associated with injection drug use behaviors and HCV independently, the present findings illustrate that the patterns of drug use among older and younger AA differ significantly and may influence health outcomes.
Financial Support: This study was supported by RIMI-COR grant R01DA014498

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PREVALENCE AND CORRELATES OF NONMEDICAL PRESCRIPTION OPIATE AND NONMEDICAL PRESCRIPTION SEDATIVE USE AMONG A GROUP OF ADOLESCENTS AND YOUNG ADULTS WITH CURRENT DRUG USE IN AN URBAN EMERGENCY DEPARTMENT.

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Aims: Nonmedical prescription drug use, defined as using opiates or sedatives to 'get high', taking someone else's or taking more than was prescribed, is a major public health problem. The aims of this analysis are to 1) identify the prevalence of nonmedical prescription opiate use (NPOU) and nonmedical prescription sedative use (NPSU) and the prevalence of dependence and abuse among a population of youth with current drug use, and 2) Identify correlates of lifetime NPOU and NPSU.
Methods: Patients age 14-24 presenting to an urban ED for care between 2/2010 and 9/2011 were recruited as part of a larger study. Recruitment occurred systematically, and those reporting any drug use in the past 6 months completed a survey using validated measures and a chart review was performed to ascertain ED visit characteristics. Patients presenting with a violent injury were oversampled. Correlates of lifetime NPOU and NMPSU were examined using logistic regression.
Results: Of 1,448 participants screened, 600 (41%) endorsed past 6-month drug use. Among this sample, 16.5% (n=99) reported lifetime NPOU, and 67% of those (n=63) reported NPOU in the past 6 months. Similarly, 20% (n=118) of the sample endorsed lifetime NPOU and 59% of those reported NPSU in the past 6 months. Among those with lifetime NPOU or NPSU, 28% met criteria for dependence or abuse and 42% were at moderate or high risk for problems related to prescription opiates or sedatives respectively. Correlates of lifetime NPOU included identifying as Caucasian and cocaine use. Correlates of lifetime NPSU included Caucasian race, cocaine use, current depression, alcohol misuse and peer violence.
Conclusions: Among adolescents and young adults that have used drugs in the past 6 months, NPOU and NPSU is common, with over 25% meeting criteria for dependence and abuse.
Financial Support: NIDA R01DA024646

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CHANGES IN THE AGE DISTRIBUTION OF ADMISSIONS TO SUBSTANCE ABUSE TREATMENT FOR OPIOID ABUSE IN THE U.S. FROM 2000 TO 2010.

J C Willis, Howard Chilcoat; Risk Management and Epidemiology, Purdue Pharma, L.P., Stamford, CT

Aims: In recent years there have been substantial increases in substance abuse treatment episodeswith opiates as the primary drug of abuse in the US. This study examines changes in the age distribution and associated characteristics of these individuals over time.
Methods: Data from the 2000 and 2010 Treatment Episode Data Set (TEDS) were used to estimate the numbers of people entering treatment with prescription opioids as primary drug of abuse in publicly funded treatment centers in the US. Trends in the numbers and distributions over time were compared by age, as well as characteristics including route of administration, source of referral and frequency of use.
Results: Number of treatment entries increased 5-fold from 2000 to 2010. There was a shift in the distribution towards younger ages in more recent surveys. In 2000, peak prevalence was in 35-39 year olds versus 25-29 year olds in 2010. 58% of people entering treatment in 2000 were above age 35 compared to 28% by 2010. In contrast, 31% of people entering treatment in 2010 were under age 25 versus 13% in 2000. There was a difference in the primary route of administration by age between 2000 and 2010: 14% of 18-20 year olds reported inhalation as their primary route in 2000 as compared with 35% in 2010. In contrast patterns of injecting showed little change over time, with 16% of 18-20 year olds reporting injection as their primary route. Adolescents were more likely to be infrequent users than older individuals with little change in patterns of frequency by age over time. Criminal justice was a major source of referral for younger age groups, 23% of people under age 20 were referred via criminal justice in 2010.
Conclusions: Between 2000 and 2010 there was a large increase in treatment episodes among younger individuals, who are less likely to represent patients who were taking the medicine as directed following a prescription. The differences in the characteristics of younger compared to older patients require different prevention and treatment strategies to address the changing age demographics.
Financial Support: Funded by Purdue Pharma, L.P.

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A RANDOMIZED CLINICAL TRIAL EVALUATING THE IMPACT OF CONCURRENT OUTPATIENT SMOKING-CESSATION AND SUBSTANCE USE DISORDER (SUD) TREATMENT ON SUBSTANCE USE OUTCOMES.

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Aims: To evaluate the impact of SUD treatment as usual plus smoking-cessation treatment (TAU+SCT), relative to SUD treatment as usual (TAU), on substance use outcomes in cocaine and/or methamphetamine-dependent patients.
Methods: This was a 10-week NIDA CTN trial with follow-up at 3 and 6 months post-smoking quit date. A total of 538 stimulant-dependent patients who wished to stop smoking cigarettes were recruited from 12 sites. TAU participants received SUD treatment as usual. TAU+SCT participants received weekly individual smoking-cessation counseling and extended-release (XL) bupropion (300 mg/day) during weeks 1-10. During the post-quit treatment phase (weeks 4-10), TAU+SCT participants received the nicotine inhaler and contingency management for smoking abstinence. Efficacy measures included stimulant, any drug, and cigarette use.
Results: A total of 479 participants (i.e., 89%) completed the 10-week treatment phase. Stimulant use was relatively low and there were no significant treatment effects for stimulant-use outcomes. TAU+SCT, relative to TAU, participants had significantly better point-prevalence smoking abstinence (e.g., at week 10, $X2(1)=44.69$, $p<.001$). There were no significant treatment effects for complete drug-abstinence but the TAU+SCT, relative to TAU, participants showed a consistently greater increase in drug-free days across the trial (two-sided binomial sign test $p<.001$), with a trend for a significant treatment difference during active treatment ($X2(1)=3.61$, $p=.058$), and a significant difference at 6-month follow-up ($X2(1)=4.09$, $p<.05$).
Conclusions: SCT for stimulant-dependent patients in outpatient SUD treatment did not significantly improve stimulant-use outcomes, increased smoking abstinence and drug-free days.
Financial Support: National Institute on Drug Abuse, Center for Clinical Trials Network

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THE ASSOCIATION BETWEEN ADHD AND NICOTINE IN A PROSPECTIVE SAMPLE OF YOUTH.

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Aims: To describe pattern of nicotine involvement (age of onset, frequency and dependence symptoms) in a relatively large, community-identified sample of children with ADHD who have been assessed longitudinally from childhood through late adolescence (up to age 22).
Methods: We present findings from our multi-dimensional and standardized follow-up assessments at waves 4, 5 and 6 (ages 18 – 22). Three rigorously diagnosed groups that were epidemiologically identified during childhood in 1991: ADHD-externalizing (n=90), ADHD-only (n=29), and matched controls (n=93). The follow-up battery consisted of standardized measures of nicotine involvement.
Results: After controlling for the effects of the covariates (stimulant medication and education level), we found that the childhood ADHD-externalizing (oppositional defiant disorder or conduct disorder) group was significantly associated with higher levels of nicotine use, a greater number of nicotine dependence symptoms, and an earlier onset of nicotine use compared to the ADHD-only and control groups (all levels of significance > .01). These findings were found at all three time points and in both boys and girls.
Conclusions: The results of the present study indicate that individuals who met diagnostic criteria for ADHD with an externalizing disorder as a child reported a higher rate of nicotine use and more nicotine addiction symptoms during their late adolescent and young adult years when compared to individuals in the ADHD-only and non-ADHD groups. This major finding is consistent with both the general drug abuse risk literature that the relation between ADHD and substance use, including nicotine, outcomes may be partially or fully accounted for by the co-existence of ADHD and externalizing disorders. Thus, the study results support the view that ADHD without an externalizing disorder does not give rise to additional risk for nicotine use beyond the risk found in non-ADHD youth, a pattern that held across the late adolescent and young adulthood data points.
Financial Support: This study was supported by grants K02 DA015347 and R01 DA0112995 from the National Institute on Drug Abuse.

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EVIDENCE OF A META-MEMORY DEFICIT AMONG CHRONIC METHAMPHETAMINE USERS.

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Aims: Chronic methamphetamine (MA) use is associated with moderate deficits in learning and memory; poor awareness of these deficits may increase the risk of errors in real-world outcomes (e.g., automobile driving). The current study evaluated the hypothesis that MA use is associated with decreased awareness of memory deficits, as has been observed in other clinical populations in which prefrontal neural systems are injured.
Methods: 195 participants with lifetime MA dependence diagnoses and 195 non-MA-using comparison subjects underwent comprehensive neuropsychiatric research assessments, including performance-based and self-report measures of episodic memory.
Results: MA diagnosis was independently associated with lower scores on performance-based measures of visual and verbal learning and memory, as well as elevated memory complaints in daily life (ps<.05). The concordance between performance-based and self-report of memory problems was lower in the MA group (44% accurate) versus non-users (63% accurate), independent of other clinical factors, including current depressive symptoms (p<.05). Within the MA group, meta-memory inaccuracy was uniquely associated with higher rates of dependence in instrumental activities of daily living and psychomotor slowing (ps<.05).
Conclusions: Chronic MA use is associated with reduced awareness of objective deficits in memory acquisition and retention, including both over- and under-evaluations of current levels of memory functioning that may increase concurrent risk of disability in normal daily activities. Cognitive neurorehabilitation efforts to enhance meta-memory accuracy and deployment of appropriate compensatory mnemonic strategies may confer some benefits for substance abuse treatment outcomes.
Financial Support: The authors report no conflicts of interest. This research was supported by National Institutes of Health grants T32-DA31098, P01-DA12065, P50-DA026306, L30-DA032120.

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BUPRENORPHINE-NALOXONE VS. METHADONE: EQUAL HIV RISK REDUCTION IN START.

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Aims: Aims: Compare reductions in HIV injection and sexual risk behaviors in patients treated with methadone (MET) or buprenorphine-naloxone (BUP).
Methods: Methods: Secondary analysis of HIV risk from a study aimed to evaluate transaminase differences following randomization to a 6-month course of MET or BUP in nine methadone programs participating in the NIDA Clinical Trials Network. Participants were consenting, treatment seeking, opioid addicted individuals who remained in their assigned condition for 24 weeks and had 4 or more monthly blood draws. The Risk Behavior Survey measured past 30-day HIV risk at baseline and at weeks 12 and 24.
Results: Results: Among 731 evaluable participants (BUP=340; MET=391), 700 completed the 12 -week follow-ups and 705 completed 24-week follow-ups. Highly significant reductions in injecting risk (p< 0.0001) were seen across time in both groups with no differences between groups in the number of times heroin, speedball, or other opiates were injected and the total times injected. Additionally, there was no difference in the times needles shared, times needles were not cleaned with bleach prior to sharing, shared cooker, engaged in front/back load, and needle risk composite score. Less pronounced, but also significant (p< 0.03-0.05) were reductions seen in the number of multiple sex partners, instances of unsafe sex and sex risk composite score, with more reduction of the sex risk composite (p< 0.05) in MET than BUP patients.
Conclusions: Conclusions: Equal and marked reductions in HIV injecting risk, with significant but less striking reductions in sex risk occurred among patients who remained on BUP and MET.
Financial Support: DA U10 - 013043 NIDA

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GENDER DIFFERENCES IN SUBSTANCE USE TREATMENT UTILIZATION THE YEAR PRIOR TO DEPLOYMENT IN ARMY SERVICE MEMBERS.

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Aims: The impact of the current wars on Army veterans has increased concerns about substance use (SU) and the need for SU treatment (SUT). Gender may be important for understanding SUT utilization before deployment given both gender differences and similarities in military and deployment experiences. This study examined gender differences in SUT utilization the year prior to deployment for Army service members to determine: the rates of substance use diagnosis (SUDX) and SUT before deployment and if the odds of receiving military-provided SUT the year before deployment differ by gender.
Methods: A retrospective cohort design was used to analyze military health system claims data to examine gender differences in both substance use diagnosis (SUDX) and SUT in 152,447 Army service members who returned from deployments in FY2010.
Results: Propensity score analysis indicated that women had lower odds (AOR: 0.91, 95% CI: 0.86-0.96) of military lifetime SUDX. After adjusting for factors of the Gelberg-Andersen Behavioral Model for Vulnerable Populations and military lifetime SUDX in logistic regression, women also had lower odds (AOR: 0.61; 95% CI: 0.54-0.70) of using SUT the year prior to deployment.
Conclusions: Army women may have reduced access to SUT the year prior to deployment compared to men, even after controlling for epidemiological differences associated with gender. Findings suggest gender disparities in military-provided SUT, and the need for military leaders and SUT professionals to consider whether military SU assessment protocols are sensitive to gender differences.
Financial Support: NIDA #R01DA030150; Data sponsorship from DHCAPE. The opinions or assertions herein are those of the authors and do not necessarily reflect the view of the US Army, Department of Defense.

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SOCIAL NETWORK DRINKING FREQUENCY MODERATES THE EFFECTS OF NALTREXONE ON HEAVY DRINKING DAYS IN THE COMBINE STUDY.

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Aims: Previous studies largely support the efficacy of naltrexone for treatment of alcohol dependence, but small effect sizes and variability in response have decreased enthusiasm for its clinical utility. Identification of characteristics that influence response to naltrexone will clarify individual differences in medication response. Via mechanisms of reducing craving and blunting reward, the relative value of naltrexone may be influenced by social exposure to alcohol. We examined whether the effects of naltrexone on within-treatment drinking outcomes were moderated by frequency of social network drinking.
Methods: Participants were adults enrolled in the COMBINE study, a multisite study of pharmacological and behavioral interventions for alcohol dependence, who completed the intake Important People Inventory (N=1,362, M age=44.43, 69% male). A dichotomous variable coded whether at least one social network member was a "weekly drinker." Hierarchical linear models examined monthly percent heavy drinking days (PHDD) from intake to end-of-treatment. Predictors were treatment condition (naltrexone vs. other), network weekly drinking, and their interaction, controlling for covariates.
Results: Most participants (81%) reported at least one weekly drinker in their network. Active naltrexone predicted lower PHDD (-3.79, p < .001) compared to other treatment conditions. Network weekly drinking did not predict greater PHDD (2.05, p = .12), but there was a significant interaction of network weekly drinking with naltrexone (-5.59, p < .05), such that active naltrexone led to relatively greater reductions in PHDD for participants with weekly drinkers in their social network.
Conclusions: Naltrexone may have greater clinical value in the context of greater exposure to alcohol. Social network drinking is potential marker for clinical use of this medication, in addition to those identified (e.g., OPRM1) in prior research.
Financial Support: NIDA, NIAAA

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INTERACTIONS BETWEEN OPRK1VARIANTS AND CUMULATIVE STRESS ARE ASSOCIATED WITH BASAL ACTH IN HEALTHY COMMUNITY SUBJECTS.

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Aims: Kappa opioid receptor (OPRK1) regulates stress response via the hypothalamic-pituitary-adrenal (HPA) axis. OPRK1 and stress responses are associated with addiction vulnerability. Cumulative adverse events increase risk of addiction and alter HPA activity. Thus, we investigated the interaction of OPRK1and cumulative adversity index (CAI) on HPA measures of basal morning levels of adrenocorticotropic hormone (ACTH) and cortisol in healthy subjects.
Methods: Six hundred eighty-six healthy subjects from New Haven, CT were recruited for the study. Each subject was interviewed by using CAI and blood was drawn for genotyping. CAI is a comprehensive measure with a total of 140 items covering chronic stress, major and recent life event, and life trauma. A total of 31 SNPs were genotyped. Linkage disequilibrium was estimated by using D'. Cortisol and ACTH levels were measured by using standard RIA methods. Generalized liner model (GLM) was used to analyze interaction between SNP and CAI covariates for age, race, gender and years of education. P value was adjusted by using false discovery rate (FDR).
Results: All SNPs met HWE. No association of single SNP with ACTH and cortisol was found. Two haplotype blocks were defined. Six out of 13 SNPs in one block showed significant interaction with CAI on ACTH level (FDR p=0.02 for rs12056411; p=0.02 for rs6985052; p=0.02 for rs16918934; p=0.02 for rs2303433; p=0.03 for rs997917; p=0.02 for rs782201). More interestingly, minor alleles of 6 SNPs interacting with lower CAI score were significantly associated with higher ACTH levels. NO effects were seen for cortisol levels.
Conclusions: Our results suggest that OPRK1 variants interact with adverse life events to affect variation in morning HPA axis activity in healthy subjects. The impact of these results on drug use and abuse will be the focus of future work.
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MIGRATION AND TOBACCO SMOKING BY RACE-ETHNICITY SUBGROUPS IN THE U.S.

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Aims: For some subpopulations, migration into the United States (US) may be followed by increases in tobacco smoking behaviors, toward higher US estimates. Contrariwise, some countries have higher smoking prevalence than the US; there might be attenuation of smoking prevalence among in-migrants relative to the US-born. Given a history of generally higher tobacco smoking estimates in some Asian countries (e.g., Japan), we cross-classified young Japanese-American (JA) community residents by whether they had been born in US or in Japan, with an expectation that the tobacco smoking estimates might be larger for the Japan-born in-migrants relative to the US-born JA. The evidence reported here includes smoking prevalence estimates for previously unexamined race-ethnicity (RE) subgroups within US population, as well as migration hypothesis-testing.
Methods: Data are from R-DAS datasets for 2002-9, all based on nationally representative community sample surveys within the US, including computerized assessment of RE, age, and current smoking (past 30 days), all via standardized items. Estimates are from R-DAS weighted analyses with variance estimation for complex survey data.
Results: Exploratory analyses marked the youngest JA subgroup (12-30 yr olds) as having one of the largest estimates for current smoking prevalence (27%; 95% CI: 23%, 32%) versus other subgroups of this age: Chinese, 13%; Asian Indian,12%; Filipino, 22%; Vietnamese, 18%. With respect to the targeted migrant hypothesis, for 12-30 yr old Japan-born JA, estimated prevalence is 32%, for US-born JA counterparts, the corresponding estimate is 25% — i.e., noteworthy but not statistically significant. Note that 47% of Japan-born 12-30 yr old JA males were current smokers, as compared to 28% of the US-born JA.
Conclusions: Against a background of remarkably large smoking prevalence estimates for some youthful subgroups in US, this study provides a range of novel estimates that are pertinent to 21st century tobacco control policies, and sets a stage for new research on migration and smoking.
Financial Support: T32DA021129 (WX); MSU(CLQ); K05DA15799 (JCA)

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SEX/GENDER DIFFERENCES AND THE IMPACT OF RISK FACTORS AND PSYCHOSOCIAL FUNCTIONING ON THE TIME TO RE-ARREST AMONG OFFENDERS TREATED FOR SUBSTANCE USE.

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Aims: The primary aim of the current study is to explore sex/gender differences on the relationships of pre-treatment risk factors (i.e., substance use severity and criminal history) and psychosocial functioning (i.e., decision making, self-esteem, and peer support) with time to re-arrest following termination from prison.
Methods: Survival analysis was used to model time to re-arrest in terms of pre-treatment risk factors and psychosocial functioning and to study their interaction with sex/gender. The sample consisted of 694 participants (384 males and 310 females) who were admitted to four prison-based substance abuse treatment programs. Substance use severity, criminal history, decision making, and self-esteem were measured at treatment intake. Peer support from treatment cohorts was measured at the end of orientation (approximately 1 month after intake).
Results: Decision making and peer support were positively associated with male participants' time to re-arrest, indicating that male inmates who self-report having good decision making skills and more peer support had a longer time until re-arrest. However, self-esteem and substance use severity were negatively associated with the time to re-arrest, suggesting that male inmates with relatively high self-reported self-esteem and more severe substance-related problems were re-arrested sooner than their counterparts. For female participants, criminal history was the only predictor that impacted the time to re-arrest; female inmates with more self-reported criminal involvements were re-arrested sooner than those with less criminal involvements.
Conclusions: Decision making, peer support, self-esteem, and substance use severity predicted the time to re-arrest for male participants, whereas criminal history predicted the time to re-arrest for female participants. Clinical implications include the importance of enhancing decision-making ability and peer support, and addressing addiction-related problems.
Financial Support: NIDA/NIH R01DA025885, 5U01DA016190.

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CONCURRENT CHOICE BETWEEN CUES FOR SOCIAL INTERACTION AND AMPHETAMINE IN ADOLESCENT MALE AND FEMALE RATS.

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Aims: The current study examined choice between social interaction and amphetamine (AMPH) using conditioned place preference (CPP) in individually- and pair-housed adolescent male and female rats. Group-housing has been shown to attenuate the rewarding effects of social interaction and to enhance drug CPP. Also, social interaction has been shown to be more rewarding in males relative to females. Thus, the hypothesis was that pair-housed rats would spend more time in an environment previously paired with AMPH, whereas individually-housed males, but not females, would prefer an environment paired with social interaction.
Methods: Twenty-four male and 12 female Sprague Dawley rats were allowed to explore a three-compartment CPP apparatus during a 15-min session at postnatal day 28. Individually- or pair-housed rats received four conditioning sessions in which social interaction with a sex-matched conspecific was paired with one side of the CPP chamber and four sessions in which injections of AMPH (1 mg/kg) were paired with the other side of the CPP chamber. Following conditioning, rats were allowed to explore both ends of the CPP chamber. A preference ratio was calculated. A ratio of 0.5 indicated no preference for either compartment. One-sample t tests were performed to determine if each preference ratio was significantly different from 0.5.
Results: Individually-housed male rats spent more time in the compartment previously paired with social interaction, whereas pair-housed male and females spent more time in the compartment paired with AMPH. Individually-housed females did not develop a preference for either compartment.
Conclusions: These results indicate that the therapeutic effects of social interaction in a preclinical model are enhanced in males, but not females, when housed individually during adolescence. Thus, while both males and females are sensitive to AMPH reward during adolescence, males are more sensitive to the effects of social isolation.
Financial Support: NIH grants P50 DA05312 and T32 DA016176.

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IS OXYCONTIN A SPECIAL TRIGGER FOR NEWLY INCIDENT HEROIN USE?

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Aims: Newly reformulated Oxycontin (OXY) products might cause newly incident heroin use (NIHU). We aim to estimate the degree to which NIHU might depend upon prior extra-medical OXY use in 2002-9, among young adults, before reformulation in 2010, using comparator drug compounds intended to shed light on the association's specificity. (Here, 'extra-medical' means use beyond boundaries of prescribers' intent, EM).
Methods: Data are from R-DAS online analyses consolidated from 2002-2009 National Surveys on Drug Use & Health (NSDUH, n>500,000), designed to yield nationally representative samples of US non-institutionalized community residents age 12+ years. The response of interest is NIHU between 18-25 yrs, as might be determined by early-onset drug use (<age 18). Estimation accounts for weights and clustering.
Results: Among 18-25 year olds with no history of EM drug use < age 18, NIHU > 18th birthday was quite rare (0.7%). A corresponding estimate for NIHU among early-onset EM OXY users was 8.7%, a 12-fold excess. As for other comparators, this estimated risk ratio (RR) was not exceptional, with similar RR estimates for cocaine (9.5) and psychotherapeutic drugs (~8); lower RR for pain relievers (5.5); cannabis (3.1); tobacco (2.3); alcohol(2.0).
Conclusions: Of note is an estimated 0.7% heroin use incidence at 18-25 years (with no prior EM drug use), as are these RR estimates. If indeed post-2012 re-formulation is triggering NIDU, future OXY-heroin estimates should be larger than RR=12. These RR estimates are time-lagged: early EM use before 18 years, and later NIHU between 18-25 years. A next step is a case-crossover analysis, shedding light on RR estimates for a more rapid triggering of NIHU after OXY or other drug use.
Financial Support: K05DA015799 (JCA); HHY is 1st year predoctoral fellow in Epidemiology Training Program at Michigan State University.

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A PILOT STUDY EXAMINING THE EFFICACY OF VIRTUAL-REALITY-BASED RELAPSE PREVENTION AMONG ALCOHOL-DEPENDENT VETERANS WITH TRAUMATIC BRAIN INJURY.

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Aims: To evaluate the efficacy of cognitive-behavioral therapy in conjunction with virtual-reality based relapse prevention on alcohol consumption and craving among treatment-seeking veterans with traumatic brain injury and/or post-traumatic stress disorder.
Methods: Participants (n=6) were enrolled in the study. Final analyses are based on the 4 that completed treatment. Treatment sessions were conducted once a week for 8 weeks with 1- and 3-month follow-up visits. Sessions consisted of a 30 minute cognitive-behavioral therapy session supplemented with virtual-reality scenarios as needed. A standard virtual-reality cue reactivity session was also conducted at baseline, week 4, and week 8.
Results: An increase in the self-reported number of days abstinent in the past week was observed from baseline (2±1.2; mean±SEM) by week 8 (4.5±1.7). While the increase was not significant, these levels were maintained through 3-months follow-up (5±1.1). Significant decreases in visual analog scale measures of "Craving a Drink", "Getting a Drink", "Next Time I will Drink", "Buy a Drink", and "Urge or Desire to Drink" were observed at week 8 relative to baseline and these differences were maintained at follow-up visits. Finally, a significant Time X Condition interaction was observed during cue-reactivity sessions with cue-induced craving levels decreasing more rapidly after being exposed to alcohol-related cues relative to neutral cues ($F2,12 = 4.3$, $p = .04$).
Conclusions: Despite the small N of the current pilot study, the observed improvements in drinking and craving indicate that cognitive-behavioral therapy in conjunction with virtual-reality shows great promise as a potential treatment for this population.
Financial Support: Funding provided by the Michael E. DeBakey VA Medical Center Traumatic Brain Injury Center of Excellence. This work was conducted at, and supported by the Michael E. DeBakey VA Medical Center, Houston, TX

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BACLOFEN, A GABA B AGONIST, REDUCES RISK-TAKING AND REVEALS THE RELATIONSHIP BETWEEN BRAIN RESPONSES TO DRUG CUES AND RISK-TAKING IN COCAINE-ADDICTED PATIENTS.

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Aims: Cocaine addiction is associated with the display of high-risk behaviors despite potential negative consequences. We examined the effects of baclofen (BAC)—a GABA B agonist known to modulate motivation in the context of drug reward—on risk-taking in cocaine-addicted patients. We also examined the relationship between the neural response to cocaine cues and risk-taking. We hypothesized that risk-taking would be 1) reduced in BAC-treated patients and 2) positively related to the neural response to drug cues in regions involved in the evaluation of reward and risk.
Methods: Patients were randomized to receive BAC (20mg t.i.d.; n=8) or placebo (PBO; n=10). Risk-taking behavior was assessed in the first week of treatment using the Balloon Analogue Risk Task (BART). Between days 7-10 of treatment, event-related BOLD fMRI was used to measure brain responses to cocaine-related and comparison cues. Regression analysis was used to examine correlations between brain responses to cocaine cues and BART scores.
Results: Risk-taking behavior was lower in BAC- than PBO-treated patients ($t=2.16$, $p<0.05$). In both groups, risk-taking was positively correlated with caudal orbitofrontal cortex (OFC) and amygdala activation in response to cocaine cues. In the BAC group only, inverse correlations were also observed between risk-taking and lateral OFC activation.
Conclusions: This is the first demonstration that a GABA B agonist reduces risk-taking. These results also provide the first neurophysiological evidence that drug cue reactivity is associated with risk-taking in addicted individuals. As risk-taking was inversely related to lateral OFC reactivity in BAC-, but not PBO-treated patients, our data suggest that BAC may enhance reward valuation processes to reduce risky behavior and could therefore reduce the likelihood of relapse.
Financial Support: NIDA T32 DA028874, P50 DA12756, Commonwealth of Pennsylvania CURE Addiction Center of Excellence

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SUBSTANCE USE AND PTSD AMONG SMOKERS WITH SERIOUS MENTAL ILLNESS.

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Aims: Aims: Epidemiological studies indicate Posttraumatic Stress Disorder (PTSD) frequently co-occurs with substance use and abuse, particularly among women. This study examined the PTSD-substance use relation in a sample of men and women smokers with serious mental illness.
Methods: Methods: 733 adult smokers (51% male) aged 18-73, were recruited from 5 acute inpatient psychiatry units. The e-MINI measured PTSD. Past 30-day substance use and readiness to change were assessed for heavy alcohol use (ALC), stimulants (STIM), sedatives (SED), hallucinogens (HAL), opiates (OP), and marijuana (MJ). The SF-12 assessed physical and mental health functioning. Logistic regression analyses tested for women and men separately the relation of PTSD with substance use and readiness to change.
Results: Results: 44% of women and 36% of men had PTSD. Past 30 day use of ALC, STIM, SED, OP and MJ was high (women range: 21.5% to 39.6%, men range: 24.9% to 47.1%). HAL use was lower (women: 3.9%, men: 5.9%). On average, women used 1.6 (sd=1.2) and men used 1.7 (sd=1.2) substances, during the past 30 days. Adjusting for covariates, use of OP (OR=2.1, p=.01), SED (OR=1.8, p=.02), and MJ (OR=1.9, p=.01) predicted PTSD in women. Use of STIM (OR=1.8, p=.04) and MJ (OR=1.7, p=.04) predicted PTSD in men. Number of substances used predicted PTSD in women (OR=1.5, p<.01), but not men. PTSD was unrelated to motivation to quit ALC/drugs. PTSD and # of substances used were associated with poorer mental health functioning, and a significant interaction indicated mental health functioning was the worst among those with both PTSD and greater substance use (b=2.1, p=.03).
Conclusions: Conclusions: Among smokers with serious mental illness, recent heavy alcohol, illicit drug use, and PTSD were common, found to co-occur, and predictive of worse mental health functioning. Integrative treatments for PTSD and substance abuse, with attention to sex-specific drugs of abuse, appear warranted.
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WHAT MEDICAL CARE NEEDS OF HOMELESS AND HOUSED VETERANS ARE SERVED BY THE VA?

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Aims: Homeless persons have multidimensional medical needs and high rates of substance use disorders (SUD) and mental illness. Housing First models can improve homeless persons' treatment engagement and SUD outcomes. The Department of Housing and Urban Development (HUD) – Veterans Affairs (VA) Supportive Housing (HUD-VASH) Program provides housing vouchers and case management to homeless Veterans. We apply the Behavioral Model for Vulnerable Populations to understand differences in diagnoses for which Veterans receive care across four groups: HUD-VASH, currently homeless, housed low-income and other housed. To describe and contrast VA patients according to their housing and income status and their diagnoses. We hypothesize that HUD-VASH Veterans receive more diagnoses for SUD, mental illness and chronic physical illness than all other Veterans.
Methods: We analyzed the Veterans Health Administration Outpatient Medical SAS Data restricted to outpatient ambulatory care medical visits made at the VA Greater Los Angeles Healthcare System between 10/1/10 and 9/30/11. The analyses are based on 74,858 unique patients with a total of 938,259 visits. We used the $\chi 2$ test and multivariate logistic regression models.
Results: SUD, mental illness and multi-morbidities were more common in both homeless Veteran groups (VASH, homeless) than for housed (low income, other). HUD-VASH Veterans had the highest % reporting >= 1 of the following: SUD (31%, 16%, 6%, 3%), mental illness (54%, 28%, 19%, 23%), chronic physical illness (70%, 38%, 57%, 52%), tri-morbidity (20%, 6%, 2%, 1%), respectively. Controlling for demographics, HUD-VASH Veterans had higher odds of drug disorders (AOR=8.78) and alcohol disorders (AOR=6.07) than general housed Veterans.
Conclusions: HUD-VASH Veterans are treated for different diagnoses than currently homeless Veterans. There are two possible explanations: HUD-VASH Veterans may be sicker or they may utilize the VA more for their illnesses.
Financial Support: This work was supported in part by the Department of Veterans Affairs Center for the Study of Health Care Provider Behavior.

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ASSOCIATION OF THE PRODYNORPHIN GENE PROMOTER REPEAT POLYMORPHISM WITH BASAL PROLACTIN LEVEL IN NORMAL HUMAN MALE VOLUNTEERS.

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Aims: Prolactin secretion is solely under inhibitory hypothalamic tuberoinfundibular dopaminergic control in humans. Dynorphin is a powerful regulator of basal and drug-induced dopaminergic tone and therefore prolactin levels. The number of 68-bp repeats in the PDYN promoter has an effect on gene promoter activity in vitro; also, this gene polymorphism was reported to be associated with cocaine/alcohol codependence. In this study we evaluated the effect of PDYN 68-bp repeat variants on prolactin release in normal male human volunteers.
Methods: Fifty three Caucasian and 39 African American healthy normal male volunteers, consecutively ascertained from 1995 to 2011, who participated in neuroendocrine studies in the Rockefeller University Hospital and gave consent for genetic studies were examined. The region of the PDYN gene containing the 68-bp repeats was amplified and analyzed by gel electrophoresis. PDYN genotypes were grouped into short (SS, one or two copies), long (LL, three, four, or five copies), and short/long (S/L, heterozygous). Levels of serum prolactin were determined by immunoradiometric assays from blood samples drawn between 9 and 10AM on the study day at two baseline time points 10 min apart. Two-way analysis of variance, Genotype X Ethnicity, was used to examine differences in mean basal levels of prolactin.
Results: There was a significant main effect of genotype $F(2,86) = 6.31$, $p<0.005$ in prolactin levels, with no significant interaction. There was no effect of ethnicity. Higher prolactin levels were found in subjects with SS genotype (n=18) compared to SL genotype (n= 37; $p<0.05$) or LL genotype (n=37; $p<0.001$).
Conclusions: The higher prolactin levels found in subjects with the short SS genotype, who presumably had higher PDYN expression, are related to lower dopamine tone and thus relatively lower suppression of prolactin release.
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SMOKING CESSATION IN THE ELDERLY USING NICOTINE REPLACEMENT THERAPY.

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Aims: Regardless of age, quitting smoking can significantly improve health and increase life expectancy. However, data indicate that adults age 65 or older are half as likely to quit smoking as their younger counterparts. It has been hypothesized that this sub-population may require modifications to existing treatments in order to successfully quit. In order to test this hypothesize we analyzed data from a large population-based smoking cessation study (the STOP Study; www.stopstudy.ca).
Methods: The study was open to all smokers (approximately 2 million) in Ontario Canada. Eligible participants (smoking at least 10 cigarettes per day and wanting to make a quit attempt in the next 30 days) were mailed a kit containing 5-weeks of nicotine replacement therapy (patch or gum, as requested) and self-help materials. Participants were contacted for follow-up at end-of-treatment and 6-months after enrolling. For this analysis the study sample was split by age (>/= 60 and < 60). The primary outcome was 7-day point prevalent abstinence.
Results: There were 13,143 participants enrolled in the original study. Of these 1,337 (10.2%) were age 60 or older at baseline and 11,806 were younger than 60. The response rate to end-of treatment follow-up was 33.8% (n=4439) and at 6-months was 31.4% (n=4130). Abstinence rates between the two age groups were 46.3% for the older cohort (n = 289) and 45.9% for the younger cohort (n = 1750) (p=0.86, NS) at end-of-treatment and 39.5% for the older cohort (n = 174) and 49.3% for the younger cohort (n = 1818) (p=0.0001) at 6-months.
Conclusions: While we saw no evidence of a decrease in cessation rates among older smokers we did observe an increase in relapse at 6 months. Increasing relapse prevention efforts in this age group may improve longer term cessation outcomes.
Financial Support: This study was supported by the Ontario Ministry of Health Promotion and Sport

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KNOWLEDGE, PERCEPTION AND RISK BEHAVIORS FOR HIV TRANSMISSION AMONG METHADONE CLIENTS IN SHANGHAI, CHINA.

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Aims: To investigate the knowledge, perception and risk behaviors for HIV transmission among opiate users receiving methadone maintenance treatment (MMT) in Shanghai (where prevalence of HIV is ~1% and of HCV is ~60%).
Methods: We conducted 7 focus groups with 40 methadone clients from 3 MMT clinics in Shanghai. Interviews were audio taped, transcribed, and reviewed by the first author for key issues and themes.
Results: Basic knowledge about HIV and transmission risk factors was high among participants, but they considered themselves at low risk because they thought HIV was rare in Shanghai and had little motivation to learn more about HIV or change behaviors to reduce risk. Participants reported that at least occasional drug use was common during MMT—estimated 95-99% of MMT used heroin or ice—and that use of ice was increasing rapidly. Missing a methadone dose was cited as the most common reason for using heroin during MMT. They reported that sharing instruments (e.g., syringes, dissolving water, and straws) was common but didn't consider sharing syringes with acquaintances (partners, friends or relatives) dangerous and didn't know that sharing dissolving water or straws were risky. Barriers for using clean syringes included unplanned drug use and police surveillance in pharmacies. Despite recognizing unprotected sex as a transmission risk factor, they reported that condoms were rarely used in commercial sex or with close acquaintances. Participants were interested in HCV risks, which they recognized as common problem for MMT patients.
Conclusions: MMT patients in Shanghai continue with risky behaviors. Low perceived risk for HIV may limit motivation to reduce risk behaviors, suggesting that future risk reduction interventions might be improved by broadening the focus to HCV, which is recognized as a risk, in addition to HIV.
Financial Support: Supported by NIDA-IAS Fellowship; Shanghai Health Fund for Young Physicians (2007Y15); CMHC/DMHAS/State of Connecticut.

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A TONIC-PHASIC MODEL OF *nFOSB ACTION AND RELEVANCE TO ENVIRONMENTAL ENRICHMENT.*

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Aims: Previous research has shown that △FosB is induced by psychological stress or drugs such as cocaine and amphetamine, and accumulates with repeated stimulation. However, the consequences of △FosB accumulation and its influence on neuron activity are still not clear.
Methods: This project exploits the environmental enrichment paradigm to investigate molecular responses after restraint stress or cocaine using quantitative PCR, Western blot and Immunohistochemical techniques in rat brain.
Results: Our results demonstrate that △FosB protein accumulates after repeated restraint stress and that the induction of △FosB mRNA wanes with repeated exposure. Additionally, rats reared in an enriched environment show accumulation of △FosB similar to rats exposed to repeated stress. As a result of accumulation, the transcriptional response of some △FosB target genes is inhibited. Ongoing experiments are investigating additional △FosB target genes and exploring their downstream effects.
Conclusions: We use these results to formalize a tonic/phasic model where high tonic levels of ΔFosB inhibit the phasic transcriptional response to stress or drugs. Moreover, the environment enrichment paradigm is a manipulation of tonic levels of △FosB independent of drug or stress, and prior research has shown that enriched rats exhibit differential responses to stress and/or drugs compared to isolated rats. Thus, this tonic/phasic model may underlie the protective addiction and depression phenotypes shown previously.
Financial Support: DA029091

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DEVELOPMENT OF SELECTIVE OREXIN-1 RECEPTOR ANTAGONISTS.

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Aims: Orexins play a critical role in drug reward and drug-seeking and blockade of the OX1 receptor has been suggested to be a promising strategy for the treatment of drug addiction. Unfortunately, currently available orexin compounds are either mixed OX1/OX2 ligands designed to treat sleep disorders or OX1 selective ligands with undesirable pharmacological properties. To address the pressing need for potent and selective OX1 antagonist we have synthesized a series of ligands based on the tetrahydroisoquinoline scaffold, the core structure in both the dual OX1/OX2 receptor antagonist ACT-078573 and the OX2 selective antagonist TCS-OX2-29, and further explored the structural requirements for receptor subtype selectivity.
Methods: All compounds were synthesized and characterized by MS, NMR and HPLC. Target compounds were evaluated in calcium-dependent functional assays in RD-HGA16 (Molecular Devices) cell lines stably expressing either the OX1 or OX2 receptor. Select compounds were assessed in a conditioned place preference assay.
Results: A number of compounds showed low nanomolar potency at the OX1 receptor and excellent selectivity (> 100 fold) over the OX2 receptor. Several structural features that are important for OX1 activity have been identified. For instance, as the size of substituents increases at the 7-position of the tetrahydroisoquinoline the OX1 potency also increases. When tested in vivo, a compound with good in vitro potency and OX1 selectivity alone did not have place conditioning effect but blocked the acquisition of conditioned place preference to methamphetamine in rats.
Conclusions: Structure-activity relationship studies have resulted in several compounds that are potent and OX1 selective. One such compound showed promising effect against the rewarding effects of methamphetamine. These results will facilitate the development of potent and selective OX1 antagonists as medications for the treatment of drug addiction.
Financial Support: NIH grants DA032837 and DA026582.

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GENOTYPE DIVERSITY OF HCV AMONG MMT PATIENTS IN WUHAN, CHINA.

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Aims: We previously found a high rate (555/1200, 46%) of HCV seroconversion following methadone maintenance treatment (MMT) entry and consequently set out to evaluate HCV genotype diversity and identify potential networks of HCV transmission among MMT patients in Wuhan
Methods: HCV RNA was extracted from blood specimens from a sample of 84 HCV seroconverters. The samples were analyzed using real-time PCR; HCV RNA was amplified by reverse-transcription PCR with primers targeting the 5'-untranslated and core region (5'-UTR/Core) and then sequenced for computation of phylogenetic tree and genetic distance
Results: HCV seroconverters were 67% male, with a median age 39 years and median duration of drug use of 9.5 years; 64% had less than high school education; 80% reported a history of injection drug use (IDU). Genotype 3b was predominant (34, 41%) followed by 6a (30, 36%), 3a (9, 11%), 1b (9, 11%) and 1a (2, 2%). Genotype 6a was associated with age > 30 years ($p<.05$), and IDU was associated with higher HCV RNA concentration (5.7X106 vs 3.3 X 106 IU/ml, $p<.01$). Inspection of phylogenetic tree color-coded by the patient's clinic location indicated genotype clustering according to geographical location; genetic distances of 0.0 and homogeneity index >98 were found for 6 2-person cluster and 1 3-person cluster of patients, with all patients in a cluster coming from the same clinic or district
Conclusions: Genotype 3 and 6 are most prevalent among MMT patients who seroconvert. Geographical clustering of cases with high genetic homogeneity suggests direct transmission of the virus among seroconverters, who may have continued illicit drug use following MMT admission. Further research is required to examine specific risks, behavioral factors, and transmission routes of HCV among MMT patients in Wuhan to implement more effective prevention and treatment strategies
Financial Support: CDC, Wuhan, China; NIDA DA026797 & CMHC/DMHAS/State of Connecticut

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INVOLVEMENT OF KOP-R IN COCAINE WITHDRAWAL-INDUCED CONDITIONED PLACE AVERSION IN RATS.

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Aims: Drug withdrawal-associated CPA is a test that is sensitive to the function of brain aversive systems and has been used to measure the expression of negative motivational symptoms of opiate withdrawal. However, CPA induced by cocaine withdrawal (CW) has not been established. Here we developed a paradigm of CW induced CPA (CW-CPA) and characterized this model with kappar opioid receptor (KOP-r) antagonist nor-BNI. We also tested social behavior in CW.
Methods: Rats were exposed to chronic escalating-dose (3x15-30 mg/kg at 1-h intervals from day 1 to 14) or steady-dose (3x15 mg/kg/day for 14 days) "binge" cocaine administration. The conditioning phase began on day 10, 30 min before "binge" injections (20 h after the last "binge" cocaine), and lasted for 5 days to day 14. During CW conditioning, rats were randomly assigned and confined to one conditioning chamber for 30 min. In post–conditioning test, rats were allowed free access to both chambers for 30 min on CW day 1 to 3 (acute), day 14 (chronic) or day 28 (protracted). For social behavior, we used a social investigation paradigm and assessed spatial preference and anxiety-like behaviors relative to an unfamiliar large male conspecific (with plexiglass partition) during acute CW.
Results: 1) Rats expressed the CW-CPA following CW from chronic "binge" escalating-dose, but not steady-dose, regimen; 2) The CW-CPA had an onset in acute CW, persisted into chronic CW, and returned to baseline after protracted CW; 3) Pretreatment with norBNI in acute CW reversed the CW-CPA at 5 mg/kg, but not 1 mg/kg, dose. Naloxone (mu opioid receptor anatagonist, 1 mg/kg) had no effect; 4) Nor-BNI blocked HPA activation in acute CW-CPA; 5) Preprodynorphin mRNA levels were increased in the central amygdala by acute CW-CPA; 6) Spatial preference or anxiety-like behavior was unaltered in acute CW.
Conclusions: The involvement of KOP-r in the aversive stimulus effects of the CW-CPA provides validity for the use of place conditioning as a measure to study the cocaine withdrawal-related dysphoria. Social investigation model does not serve a reliable model for CW.
Financial Support: NIDA Center Grant DA-P60-05130 (MJK)

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EFFECTS OF OREXIN RECEPTOR ANTAGONISM ON METHAMPHETAMINE-SEEKING IN MALE AND FEMALE ADOLESCENT AND ADULT RATS.

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Aims: Previous studies have shown enhanced vulnerability to addiction in adolescent (vs. adult) as well as female (vs. male) rats. The orexin system recently has been implicated in addiction and reward processing, with orexin receptor blockade more effective in reducing drug seeking in male vs. female rats. However, to date, it is not known whether there are age differences in orexin antagonism of drug seeking. In the present study, we investigated treatment of methamphetamine (METH) seeking in both adolescent (PND 23-60) and adult (> PND 90) male and female rats using selective orexin-1 receptor (Orx1A, SB-334867, 20 mg/kg) and orexin-2 receptor (Orx2A, TCS OX2 29, 20 mg/kg) antagonists.
Methods: Rats were trained to self-administer METH (0.05 mg/kg/inf, iv) during two 2-h sessions/day for 5 days. Subsequently, auditory and visual stimuli that signaled drug delivery were unplugged, and rats were allowed to extinguish lever pressing for 20 additional sessions over 10 days. Next, a within-subjects design was used to test for METH seeking precipitated by METH (1 mg/kg, ip) or METH-paired stimuli following systemic (ip) pretreatment with Orx1A or Orx2A
Results: Preliminary results indicate age differences in METH intake (adolescent > adult) and extinction responding (adult > adolescent) under these conditions. In agreement with prior work, both Orx1A and Orx2A failed to significantly reduce METH-elicited reinstatement. However, regardless of age, both Orx1A and Orx2A worked equally well to reduce METH-paired cue-elicited reinstatement in males but not females.
Conclusions: These results extend previous work to show sex-specific role for orexin signaling in cue-induced, but not METH-induced, reinstatement of METH seeking behavior.
Financial Support: Research supported by R01 DA019942-05 and K05 DA015267 (MEC).

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ASSOCIATION BETWEEN NONMEDICAL USE OF PRESCRIPTION DRUGS AND SUICIDALITY AMONG ADOLESCENTS.

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Aims: The link between drug abuse and suicidality is well established. Yet, few studies have examined the link between the nonmedical use of prescription drugs (NMUPD) and suicidality. To fill this gap in the literature, we examined associations between NMUPD and suicidality among adolescents.
Methods: Self-report data were collected from a sample of 4,178 students in grades 9-12 enrolled in five high schools. Logistic regression models were constructed for the nonmedical use of prescription pain relievers, depressants, stimulants, and a composite measure for any NMUPD. Models were estimated before and after controlling for key covariates.
Results: About 21% of respondents reported lifetime NMUPD. After covariate adjustment, students who had considered or planned a suicide were 1.3 and 1.5 times more likely to endorse any NMUPD, respectively ($p<.05$). Those who had considered suicide were 1.4 times more likely to endorse pain reliever use and 1.7 times more likely to endorse depressant use ($p<.05$). Those who planned suicide were more likely to endorse stimulants (1.6X), while reporters of suicide attempt were 1.4 times more likely to endorse depressant use ($p<.05$). Females who considered suicide were more likely to report depressant use (1.7X), while those with suicidal plans were associated with stimulant use (1.4X). Males considering suicide were more likely to report depressant (1.9X) or pain reliever use (1.7x) ($p<.05$).
Conclusions: Suicidal behaviors were significantly associated with greater odds of NMUPD for both male and female adolescents, suggesting that some adolescents may be inappropriately self-medicating psychological distress with prescription medications or NMUPD may promote suicidality.
Financial Support: Grant from Purdue Pharma L.P.

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THE MARGINAL EFFECTS OF HAZARDOUS ALCOHOL USE ON THE PROBABILITY OF BEHAVIORAL HEALTHCARE UTILIZATION AMONG NATIONAL GUARD MEMBERS.

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Aims: Utilization studies of active duty soldiers show low rates among those with alcohol problems compared to other behavioral health problems. Meanwhile, little is known about how alcohol use affects utilization during deployment among those with posttraumatic stress disorder(PTSD). The aim of this study is to estimate the marginal effect of alcohol use on the predicted rate of utilization in a National Guard population during and post-deployment.
Methods: Participants were Army National Guard service members who were surveyed approximately 2-4 months post-deployment (over 51% to Afghanistan) who had reported at least 1 symptom of PTSD, depression or hazardous alcohol use (N=236). Logistic regression models, using hazardous alcohol use(AUDIT) as a key predictor for pre-, during- and post-deployment utilization, were built by sequentially adjusting for PTSD severity, demographic characteristics, and logistical barriers. The predicted probability was derived from each logistic model; the marginal effect which measures the change in the predicted probability was obtained by taking a partial-derivative with respect to the coefficient of the alcohol variable and expressed as its ratio to the predicted probability.
Results: Preliminary results showed that hazardous alcohol use alone yielded a 21% predicted probability of behavioral health utilization, and the marginal effect indicated a 39% reduction of the utilization probability. Adding PTSD changed the effect of alcohol variable, resulting in a 69% reduction in the utilization probability due to hazardous alcohol use.Adding age, gender and logistical barriers(employment, distance to services and poor physical health) decreased the alcohol effect, yielding an overall 52% reduction in utilization probability.
Conclusions: Results suggest that hazardous alcohol use is associated with delayed utilization, especially with increases in PTSD symptoms, warranting future research to determine if alcohol use is being used as self-medication of PTSD symptoms.
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